STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 199415

TO: Ralph J Gitomer
Location: REM/3D65/3C18
Art Unit: 1655
Thursday, September 14, 2006
Case Serial Number: 10/721031

From: Toby Port
Location: Biotech-Chem Library
REM-1A59
Phone: (571)272-2523

toby.port@uspto.gov

Search Notes

Dear Examiner Gitomer,

See attached results.

If you have any questions about this search feel free to contact me at any time.

Thank you for using STIC search services!

Toby Port
Technical Information Specialist
STIC Biotech/Chem Library
(571)272-2523

```
=> file caplus; d que l7
FILE 'CAPLUS' ENTERED AT 13:15:57 ON 14 SEP 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 14 Sep 2006  VOL 145 ISS 12
FILE LAST UPDATED: 13 Sep 2006  (20060913/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html


L1   (       965)SEA FILE=CAPLUS ABB=ON  PLU=ON  PARSONS R?/AU
L2   (         7)SEA FILE=CAPLUS ABB=ON  PLU=ON  DAGHFAL D?/AU
L3   (         1)SEA FILE=CAPLUS ABB=ON  PLU=ON  LIPOWSKY C?/AU
L4   (        73)SEA FILE=CAPLUS ABB=ON  PLU=ON  WEIGAND R?/AU
L5   (       136)SEA FILE=CAPLUS ABB=ON  PLU=ON  FRIESE J?/AU
L6   (     10806)SEA FILE=CAPLUS ABB=ON  PLU=ON  NATRIURETIC PEPTIDE
L7             2 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5)
                 AND L6


=> file biosis; d que l11
FILE 'BIOSIS' ENTERED AT 13:16:10 ON 14 SEP 2006
Copyright (c) 2006 The Thomson Corporation

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 13 September 2006 (20060913/ED)


L1   (       965)SEA FILE=CAPLUS ABB=ON  PLU=ON  PARSONS R?/AU
L2   (         7)SEA FILE=CAPLUS ABB=ON  PLU=ON  DAGHFAL D?/AU
L3   (         1)SEA FILE=CAPLUS ABB=ON  PLU=ON  LIPOWSKY C?/AU
L4   (        73)SEA FILE=CAPLUS ABB=ON  PLU=ON  WEIGAND R?/AU
L5   (       136)SEA FILE=CAPLUS ABB=ON  PLU=ON  FRIESE J?/AU
L6   (     10806)SEA FILE=CAPLUS ABB=ON  PLU=ON  NATRIURETIC PEPTIDE
L11            6 SEA FILE=BIOSIS ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5)
                 AND L6


=> file medline; d que l23
FILE 'MEDLINE' ENTERED AT 13:16:17 ON 14 SEP 2006
```

```
 FILE LAST UPDATED: 13 Sep 2006 (20060913/UP).  FILE COVERS 1950 TO DATE.

 On December 11, 2005, the 2006 MeSH terms were loaded.

 The MEDLINE reload for 2006 is now (26 Feb.) available.  For details
 on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
 See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

 OLDMEDLINE is covered back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2006 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L1   (       965)SEA FILE=CAPLUS ABB=ON  PLU=ON  PARSONS R?/AU
L2   (         7)SEA FILE=CAPLUS ABB=ON  PLU=ON  DAGHFAL D?/AU
L3   (         1)SEA FILE=CAPLUS ABB=ON  PLU=ON  LIPOWSKY C?/AU
L4   (        73)SEA FILE=CAPLUS ABB=ON  PLU=ON  WEIGAND R?/AU
L5   (       136)SEA FILE=CAPLUS ABB=ON  PLU=ON  FRIESE J?/AU
L6   (     10806)SEA FILE=CAPLUS ABB=ON  PLU=ON  NATRIURETIC PEPTIDE
L23           0 SEA FILE=MEDLINE ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5)
                AND L6


=> file embase; d que l32
FILE 'EMBASE' ENTERED AT 13:16:26 ON 14 SEP 2006
Copyright (c) 2006 Elsevier B.V. All rights reserved.

 FILE COVERS 1974 TO 14 Sep 2006 (20060914/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 EMBASE is now updated daily.  SDI frequency remains weekly (default)
 and biweekly.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L1   (       965)SEA FILE=CAPLUS ABB=ON  PLU=ON  PARSONS R?/AU
L2   (         7)SEA FILE=CAPLUS ABB=ON  PLU=ON  DAGHFAL D?/AU
L3   (         1)SEA FILE=CAPLUS ABB=ON  PLU=ON  LIPOWSKY C?/AU
L4   (        73)SEA FILE=CAPLUS ABB=ON  PLU=ON  WEIGAND R?/AU
L5   (       136)SEA FILE=CAPLUS ABB=ON  PLU=ON  FRIESE J?/AU
L6   (     10806)SEA FILE=CAPLUS ABB=ON  PLU=ON  NATRIURETIC PEPTIDE
L32           0 SEA FILE=EMBASE ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5)
                AND L6


=> file wpix; d que l40
FILE 'WPIX' ENTERED AT 13:16:33 ON 14 SEP 2006
```

FILE LAST UPDATED: 11 SEP 2006 <20060911/UP>
MOST RECENT DERWENT UPDATE: 200658 <200658/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

>>> FOR FURTHER DETAILS ON THE FORTHCOMING DERWENT WORLD PATENTS INDEX ENHANCEMENTS PLEASE VISIT:
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

```
L1  (       965)SEA FILE=CAPLUS ABB=ON  PLU=ON  PARSONS R?/AU
L2  (         7)SEA FILE=CAPLUS ABB=ON  PLU=ON  DAGHFAL D?/AU
L3  (         1)SEA FILE=CAPLUS ABB=ON  PLU=ON  LIPOWSKY C?/AU
L4  (        73)SEA FILE=CAPLUS ABB=ON  PLU=ON  WEIGAND R?/AU
L5  (       136)SEA FILE=CAPLUS ABB=ON  PLU=ON  FRIESE J?/AU
L6  (     10806)SEA FILE=CAPLUS ABB=ON  PLU=ON  NATRIURETIC PEPTIDE
L40           3 SEA FILE=WPIX ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5) AND
                L6


=> dup rem l7 l11 l40

=> dup rem l7 l11 l40
PROCESSING COMPLETED FOR L7
PROCESSING COMPLETED FOR L11
PROCESSING COMPLETED FOR L40
L94           9 DUP REM L7 L11 L40 (2 DUPLICATES REMOVED)
                ANSWERS '1-2' FROM FILE CAPLUS
                ANSWERS '3-8' FROM FILE BIOSIS
                ANSWER '9' FROM FILE WPIX

=> d ibib ed ab l94 1-8; d ibib ab abex l94 1

L94  ANSWER 1 OF 9  CAPLUS  COPYRIGHT 2006 ACS on STN  DUPLICATE 1
ACCESSION NUMBER:         2005:59922  CAPLUS
DOCUMENT NUMBER:          142:107817
TITLE:                    Stable compositions for measuring human
                          natriuretic peptides
INVENTOR(S):              Parsons, Robert G.; Daghfal, David
                          J.; Lipowsky, Cherie A.; Weigand,
                          Ray A.; Friese, Judith A.
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 30 pp., Cont.-in-part of U.S.
                          Ser. No. 620,475.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
```

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005014289	A1	20050120	US 2003-721031	20031124
US 2005014287	A1	20050120	US 2003-620475	20030716
CA 2532693	AA	20050127	CA 2004-2532693	20040715
WO 2005008253	A2	20050127	WO 2004-US22866	20040715
WO 2005008253	A3	20050616		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1649290	A2	20060426	EP 2004-778404	20040715

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

PRIORITY APPLN. INFO.:	US 2003-620475	A2 20030716
	US 2003-721031	A 20031124
	WO 2004-US22866	W 20040715

ED Entered STN: 21 Jan 2005

AB The present invention relates to stable compns., including, but not limited to, calibrators, controls and test samples, that can be used in ligand-binding assays of human **natriuretic peptides**, such as immunoassays, and methods for making said compns.

L94 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2

ACCESSION NUMBER:	2005:58110 CAPLUS
DOCUMENT NUMBER:	142:107816
TITLE:	Stable calibrators or controls for measuring human **natriuretic peptides**
INVENTOR(S):	**Friese, Judith A.**; Matias, Matthew S.; **Weigand, Ray A.**
PATENT ASSIGNEE(S):	USA
SOURCE:	U.S. Pat. Appl. Publ., 24 pp. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005014287	A1	20050120	US 2003-620475	20030716
US 2005014289	A1	20050120	US 2003-721031	20031124
CA 2532693	AA	20050127	CA 2004-2532693	20040715
WO 2005008253	A2	20050127	WO 2004-US22866	20040715
WO 2005008253	A3	20050616		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1649290 A2 20060426 EP 2004-778404 20040715

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK

US 2006029982 A1 20060209 US 2005-248650 20051012

PRIORITY APPLN. INFO.: US 2003-620475 A2 20030716

US 2003-721031 A 20031124

WO 2004-US22866 W 20040715

ED Entered STN: 21 Jan 2005

AB The present invention relates to stable calibrators and controls that can be used in ligand-binding assays and methods for making said calibrators and controls. Stable liquid calibrators as well as a method of making them are claimed.

L94 ANSWER 3 OF 9 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:13065 BIOSIS

DOCUMENT NUMBER: PREV200600015653

TITLE: Development of the ARCHITECT (R) BNP assay.

AUTHOR(S): **Daghfal, D. J.** [Reprint Author]; Shih, J.; Laird, D.; Matias, M.; Melich, T.; Solbrig, T.; Billing-Medel, P.; Maggio, P.; George, S.; Hales, T.

CORPORATE SOURCE: Abbott Labs, Abbott Pk, IL 60064 USA

SOURCE: Clinical Chemistry, (2005) Vol. 51, No. Suppl. 6, pp. A18. Meeting Info.: Annual Meeting of the American-Association-for-Clinical-Chemistry. Orlando, FL, USA. July 24 -28, 2005. Amer Assoc Clin Chem.
CODEN: CLCHAU. ISSN: 0009-9147.

DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 21 Dec 2005
Last Updated on STN: 21 Dec 2005

ED Entered STN: 21 Dec 2005
Last Updated on STN: 21 Dec 2005

L94 ANSWER 4 OF 9 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:469372 BIOSIS

DOCUMENT NUMBER: PREV200400468061

TITLE: Analytical performance evaluation of the Abbott AxSYM BNP assay.

AUTHOR(S): **Daghfal, D. J.** [Reprint Author]; Kelly, P.; Foreman, P.; Taylor, V.; Black, M.; Grant, L.; McAllister, J.; **Parsons, R.**; **Lipowsky, C.**

CORPORATE SOURCE: Abbott Labs, Abbott Pk, IL, 60064, USA

SOURCE: Clinical Chemistry, (June 2004) Vol. 50, No. 6, Suppl. S, Part 2, pp. A22. print.
Meeting Info.: 56th Annual Meeting of the American Association for Clinical Chemistry (AACC). Los Angeles, CA, USA. July 25-29, 2004. American Association for Clinical Chemistry.
CODEN: CLCHAU. ISSN: 0009-9147.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 9 Dec 2004
Last Updated on STN: 9 Dec 2004

ED Entered STN: 9 Dec 2004
Last Updated on STN: 9 Dec 2004

L94 ANSWER 5 OF 9 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:469364 BIOSIS
DOCUMENT NUMBER: PREV200400468053
TITLE: Clinical performance of the AxSYM BNP assay.
AUTHOR(S): **Daghfal, D. J.** [Reprint Author]; Foreman, P.; Kelly, P.; Sanchez, B.; **Parsons, R.**; **Lipowsky, C.**; Taylor, V.; McAllister, J.; Grant, L.; Black, M.
CORPORATE SOURCE: Abbott Labs, Abbott Pk, IL, 60064, USA
SOURCE: Clinical Chemistry, (June 2004) Vol. 50, No. 6, Suppl. S, Part 2, pp. A20. print.
Meeting Info.: 56th Annual Meeting of the American Association for Clinical Chemistry (AACC). Los Angeles, CA, USA. July 25-29, 2004. American Association for Clinical Chemistry.
CODEN: CLCHAU. ISSN: 0009-9147.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 9 Dec 2004
Last Updated on STN: 9 Dec 2004
ED Entered STN: 9 Dec 2004
Last Updated on STN: 9 Dec 2004

L94 ANSWER 6 OF 9 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:2418 BIOSIS
DOCUMENT NUMBER: PREV200500002969
TITLE: Stability of BNP in whole blood and plasma.
AUTHOR(S): **Daghfal, D. J.** [Reprint Author]; **Parsons, R.**; Kelly, P.; Foreman, P.; Taylor, V.; Brooksbank, K.; Black, M.; Grant, L.; McAllister, J.; Struthers, A.; Dargie, H.; Morton, I.
CORPORATE SOURCE: Abbott Labs, Abbott Pk, IL, 60064, USA
SOURCE: Clinical Chemistry, (June 2004) Vol. 50, No. 6, Suppl. S, Part 2, pp. A3. print.
Meeting Info.: 56th Annual Meeting of the American Association for Clinical Chemistry (AACC). Los Angeles, CA, USA. July 25-29, 2004. American Association for Clinical Chemistry.
CODEN: CLCHAU. ISSN: 0009-9147.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Dec 2004
Last Updated on STN: 16 Dec 2004
ED Entered STN: 16 Dec 2004
Last Updated on STN: 16 Dec 2004

L94 ANSWER 7 OF 9 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:372352 BIOSIS
DOCUMENT NUMBER: PREV200300372352
TITLE: Development of the AxSYM B-type **natriuretic peptide** automated immunoassay.
AUTHOR(S): Brooksbank, K. J. [Reprint Author]; MacKay, R. [Reprint Author]; Taylor, V. [Reprint Author]; Milne, K. [Reprint Author]; Kelly, P. [Reprint Author]; **Lipowsky, C.**

[Reprint Author]; Gaston, S. [Reprint Author]; Matias, M. [Reprint Author]; Clark, S. [Reprint Author]; **Friese, J.** [Reprint Author]; Shih, J. [Reprint Author]; **Parsons, R.** [Reprint Author]; **Daghfal, D.** [Reprint Author]; **Weigand, R.** [Reprint Author]
CORPORATE SOURCE: Axis-Shield Diagnostics plc, Dundee, UK
SOURCE: Clinical Chemistry, (June 2003) Vol. 49, No. S6, pp. A63. print.
Meeting Info.: 55th Annual Meeting of the AACC (American Association for Clinical Chemistry). Philadelphia, PA, USA. July 20-24, 2003. American Association for Clinical Chemistry.
CODEN: CLCHAU. ISSN: 0009-9147.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Aug 2003
Last Updated on STN: 13 Aug 2003
ED Entered STN: 13 Aug 2003
Last Updated on STN: 13 Aug 2003

L94 ANSWER 8 OF 9 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:445171 BIOSIS
DOCUMENT NUMBER: PREV200200445171
TITLE: A novel assay for the measurement of plasma B-type **natriuretic peptide** by an AxSYM(R) microparticle based immunoassay with use of stable liquid calibrators.
AUTHOR(S): Kelly, P. M. [Reprint author]; Gaston, S. [Reprint author]; MacKay, R. [Reprint author]; Arthur, K. [Reprint author]; Taylor, V. [Reprint author]; Shih, J.; Matias, M.; **Friese, J.**; **Weigand, R.**
CORPORATE SOURCE: Axis-Shield, Dundee, UK
SOURCE: Clinical Chemistry, (June, 2002) Vol. 48, No. 6 Supplement, pp. A94. print.
Meeting Info.: 54th Annual Meeting of the American Association for Clinical Chemistry (AACC). Orlando, Florida, USA. July 28-August 01, 2002.
CODEN: CLCHAU. ISSN: 0009-9147.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Aug 2002
Last Updated on STN: 21 Aug 2002
ED Entered STN: 21 Aug 2002
Last Updated on STN: 21 Aug 2002

=> d ibib ab abex l94 9

L94 ANSWER 9 OF 9 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-154106 [16] WPIX
CROSS REFERENCE: 2005-120767 [13]; 2005-120768 [13]
DOC. NO. NON-CPI: N2006-133198
DOC. NO. CPI: C2006-051759
TITLE: Stable liquid calibrator or control useful in a ligand binding sample for measuring level of **natriuretic peptide** in a test sample, comprises diluent and human synthetic **natriuretic peptide.**
DERWENT CLASS: A89 B04 D16 S03

INVENTOR(S): **FRIESE, J A**; MATIAS, M S; **WEIGAND, R A**
PATENT ASSIGNEE(S): (FRIE-I) FRIESE J A; (MATI-I) MATIAS M S; (WEIG-I) WEIGAND R A
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2006029982	A1	20060209	(200616)*		33

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2006029982	A1 Cont of	US 2003-620475	20030716
		US 2005-248650	20051012

PRIORITY APPLN. INFO: US 2003-620475 20030716; US 2005-248650 20051012

AB US2006029982 A UPAB: 20060308
NOVELTY - A stable liquid calibrator (I) or control for use in a ligand binding assay for measuring the level of **natriuretic peptide** in a test sample, comprises at least one diluent and at least one human synthetic **natriuretic peptide**, and has a pH of 4-6.5.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for making (I), comprising:

(a) mixing at least one diluent with at least one human synthetic **natriuretic peptide** to form a liquid calibrator or control;

(b) measuring the pH of the liquid calibrator or control; and

(c) depending upon the pH of liquid calibrator or control measured, the pH of the liquid calibrator or control is adjusted to 4-6.5.

USE - (I) Is useful in ligand binding assays for measuring the level of a **natriuretic peptide** in a test sample (claimed).

ADVANTAGE - (I) Is stable, can be stored at a temperature of 2-8 deg. C and can be used in an assay at ambient temperature or at 30-40 deg. C (claimed). (I) Is easy to use, and avoids reconstitution or thawing prior to use.

Dwg.0/3

```
=> file caplus; d que l50; d que l51
FILE 'CAPLUS' ENTERED AT 13:18:00 ON 14 SEP 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 14 Sep 2006  VOL 145 ISS 12
FILE LAST UPDATED: 13 Sep 2006  (20060913/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html


L41       10883 SEA FILE=CAPLUS ABB=ON  PLU=ON  NATRIURETIC (1A) PEPTIDE
L42     5686097 SEA FILE=CAPLUS ABB=ON  PLU=ON  (CALIBRAT? OR MEASUR? OR
                ASSAY? OR TEST? OR IDENTIF?)
L48       44004 SEA FILE=CAPLUS ABB=ON  PLU=ON  LIQUID (3A) L42
L49           7 SEA FILE=CAPLUS ABB=ON  PLU=ON  L41 AND L48
L50           3 SEA FILE=CAPLUS ABB=ON  PLU=ON  L49 AND (ISOLATION OR ASSAY OR
                CALIBRAT?)/TI



L8  (        11) SEA FILE=CAPLUS ABB=ON  PLU=ON  STABILIZING AGENTS+PFT,NT/CT
                (L) NATRIURETIC
L9  (         5) SEA FILE=CAPLUS ABB=ON  PLU=ON  STABILITY/CT (L) NATRIURETIC
L10          12 SEA FILE=CAPLUS ABB=ON  PLU=ON  L8 OR L9
L51           4 SEA FILE=CAPLUS ABB=ON  PLU=ON  L10 AND (MEASURE? OR METHOD?
                OR CALIBRATOR)/TI NOT TRANSDERMAL/TI


=> s l50-l51 not l7
L89           5 (L50 OR L51) NOT L7

=> file biosis; d que l21; d que l61
FILE 'BIOSIS' ENTERED AT 13:18:34 ON 14 SEP 2006
Copyright (c) 2006 The Thomson Corporation

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 13 September 2006 (20060913/ED)
```

```
L12       16678 SEA FILE=BIOSIS ABB=ON  PLU=ON  NATRIURET? (1A) PEPTIDE
L13      423241 SEA FILE=BIOSIS ABB=ON  PLU=ON  (STABLE OR STABILI?)
L16         124 SEA FILE=BIOSIS ABB=ON  PLU=ON  L12 (15A) L13
L17     4456463 SEA FILE=BIOSIS ABB=ON  PLU=ON  MEASUR? OR TEST? OR ASSAY? OR
                ANALY?
L18          79 SEA FILE=BIOSIS ABB=ON  PLU=ON  L16 AND L17
L19          63 SEA FILE=BIOSIS ABB=ON  PLU=ON  L18 NOT STABLE ANGINA
L20          20 SEA FILE=BIOSIS ABB=ON  PLU=ON  L19 AND (STABILITY OR PROBNP
                OR CLINICAL OR AXSYM OR SUCROSE OR STABILIZATION)/TI
L21          19 SEA FILE=BIOSIS ABB=ON  PLU=ON  L20 NOT STABLE CORONARY/TI


L12       16678 SEA FILE=BIOSIS ABB=ON  PLU=ON  NATRIURET? (1A) PEPTIDE
L13      423241 SEA FILE=BIOSIS ABB=ON  PLU=ON  (STABLE OR STABILI?)
L16         124 SEA FILE=BIOSIS ABB=ON  PLU=ON  L12 (15A) L13
L17     4456463 SEA FILE=BIOSIS ABB=ON  PLU=ON  MEASUR? OR TEST? OR ASSAY? OR
                ANALY?
L18          79 SEA FILE=BIOSIS ABB=ON  PLU=ON  L16 AND L17
L19          63 SEA FILE=BIOSIS ABB=ON  PLU=ON  L18 NOT STABLE ANGINA
L20          20 SEA FILE=BIOSIS ABB=ON  PLU=ON  L19 AND (STABILITY OR PROBNP
                OR CLINICAL OR AXSYM OR SUCROSE OR STABILIZATION)/TI
L21          19 SEA FILE=BIOSIS ABB=ON  PLU=ON  L20 NOT STABLE CORONARY/TI
L42     5686097 SEA FILE=CAPLUS ABB=ON  PLU=ON  (CALIBRAT? OR MEASUR? OR
                ASSAY? OR TEST? OR IDENTIF?)
L53        1373 SEA FILE=BIOSIS ABB=ON  PLU=ON  L12 (10A) L42
L54      247734 SEA FILE=BIOSIS ABB=ON  PLU=ON  LIQUID?
L55          36 SEA FILE=BIOSIS ABB=ON  PLU=ON  L53 AND L54
L58          35 SEA FILE=BIOSIS ABB=ON  PLU=ON  L55 NOT L21
L60       27012 SEA FILE=BIOSIS ABB=ON  PLU=ON  LIGAND (1A) BIND?
L61           1 SEA FILE=BIOSIS ABB=ON  PLU=ON  L58 AND L60


=> s (l21 or l61) not l11
L90          19 (L21 OR L61) NOT L11

=> file medline; d que l69
FILE 'MEDLINE' ENTERED AT 13:19:18 ON 14 SEP 2006

 FILE LAST UPDATED: 13 Sep 2006 (20060913/UP). FILE COVERS 1950 TO DATE.

 On December 11, 2005, the 2006 MeSH terms were loaded.

 The MEDLINE reload for 2006 is now (26 Feb.) available. For details
 on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
 See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

 OLDMEDLINE is covered back to 1950.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2006 vocabulary.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
```

```
L22        14925 SEA FILE=MEDLINE ABB=ON  PLU=ON  NATRIURETIC PEPTIDES+NT/CT
L42      5686097 SEA FILE=CAPLUS ABB=ON  PLU=ON  (CALIBRAT? OR MEASUR? OR
                 ASSAY? OR TEST? OR IDENTIF?)
L62        10653 SEA FILE=MEDLINE ABB=ON  PLU=ON  L22/MAJ
L66        11681 SEA FILE=MEDLINE ABB=ON  PLU=ON  LIQUID (3A) L42
L67            8 SEA FILE=MEDLINE ABB=ON  PLU=ON  L62 AND L66
L69            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L67 AND UNEXTRACTED/TI


=> file embase; d que l70; d que l75
FILE 'EMBASE' ENTERED AT 13:19:49 ON 14 SEP 2006
Copyright (c) 2006 Elsevier B.V. All rights reserved.

 FILE COVERS 1974 TO 14 Sep 2006 (20060914/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 EMBASE is now updated daily.  SDI frequency remains weekly (default)
 and biweekly.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L33        12000 SEA FILE=EMBASE ABB=ON  PLU=ON  NATRIURETIC (1A) PEPTIDE
L34       377785 SEA FILE=EMBASE ABB=ON  PLU=ON  STABLE OR STABILI?
L35          108 SEA FILE=EMBASE ABB=ON  PLU=ON  L33 (15A) L34
L36           62 SEA FILE=EMBASE ABB=ON  PLU=ON  L35 NOT (STABLE (3A) HEART OR
                 CORONARY OR ISCHEMI? OR ANGINA OR PULMONARY OR EMBOLISM)
L37           23 SEA FILE=EMBASE ABB=ON  PLU=ON  L36 AND (ELECSYS OR STABIILZ?
                 OR THAW OR LEFT OR PROLONGED OR RAPID OR ATRIAL NATRIURETIC)/TI

L38           12 SEA FILE=EMBASE ABB=ON  PLU=ON  L37 AND (SCAN? OR MEASUR? OR
                 DIAGNOS? OR ASSAY? OR TEST?)
L70            5 SEA FILE=EMBASE ABB=ON  PLU=ON  L38 AND (ELECSYS OR RAPID
                 ASSAY OR ASSESSMENT)/TI



L34       377785 SEA FILE=EMBASE ABB=ON  PLU=ON  STABLE OR STABILI?
L73          349 SEA FILE=EMBASE ABB=ON  PLU=ON  (NATRIURETIC/TI (1A) PEPTIDE/TI
                 ) (10A) (SCAN? OR MEASUR? OR DIAGNOS? OR ASSAY? OR TEST?)/TI
L74           22 SEA FILE=EMBASE ABB=ON  PLU=ON  L73 AND L34
L75            4 SEA FILE=EMBASE ABB=ON  PLU=ON  L74 AND (KIT OR KITS OR
                 RADIORECEPTOR)/TI


=> => s l70 or l75
L91            9 L70 OR L75

=> file wpix; d que l82; d que l85; d que l87
FILE 'WPIX' ENTERED AT 13:21:53 ON 14 SEP 2006
COPYRIGHT (C) 2006 THE THOMSON CORPORATION

FILE LAST UPDATED:          11 SEP 2006      <20060911/UP>
MOST RECENT DERWENT UPDATE:     200658        <200658/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE
```

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

>>> FOR FURTHER DETAILS ON THE FORTHCOMING DERWENT WORLD PATENTS
INDEX ENHANCEMENTS PLEASE VISIT:
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

```
L1  (       965)SEA FILE=CAPLUS ABB=ON  PLU=ON  PARSONS R?/AU
L2  (         7)SEA FILE=CAPLUS ABB=ON  PLU=ON  DAGHFAL D?/AU
L3  (         1)SEA FILE=CAPLUS ABB=ON  PLU=ON  LIPOWSKY C?/AU
L4  (        73)SEA FILE=CAPLUS ABB=ON  PLU=ON  WEIGAND R?/AU
L5  (       136)SEA FILE=CAPLUS ABB=ON  PLU=ON  FRIESE J?/AU
L6  (     10806)SEA FILE=CAPLUS ABB=ON  PLU=ON  NATRIURETIC PEPTIDE
L40           3 SEA FILE=WPIX ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5) AND
                L6
L76         472 SEA FILE=WPIX ABB=ON  PLU=ON  NATRIURET? (1A) PEPTIDE
L77     1575921 SEA FILE=WPIX ABB=ON  PLU=ON  MEASUR? OR TEST? OR ASSAY? OR
                ANALY? OR IDENTIF?
L78          48 SEA FILE=WPIX ABB=ON  PLU=ON  L76 (10A) L77
L79     1135746 SEA FILE=WPIX ABB=ON  PLU=ON  LIQUID OR PH
L80           5 SEA FILE=WPIX ABB=ON  PLU=ON  L78 AND L79
L81           2 SEA FILE=WPIX ABB=ON  PLU=ON  L80 NOT L40
L82           1 SEA FILE=WPIX ABB=ON  PLU=ON  L81 AND LIQUID/TI
```

```
L1  (       965)SEA FILE=CAPLUS ABB=ON  PLU=ON  PARSONS R?/AU
L2  (         7)SEA FILE=CAPLUS ABB=ON  PLU=ON  DAGHFAL D?/AU
L3  (         1)SEA FILE=CAPLUS ABB=ON  PLU=ON  LIPOWSKY C?/AU
L4  (        73)SEA FILE=CAPLUS ABB=ON  PLU=ON  WEIGAND R?/AU
L5  (       136)SEA FILE=CAPLUS ABB=ON  PLU=ON  FRIESE J?/AU
L6  (     10806)SEA FILE=CAPLUS ABB=ON  PLU=ON  NATRIURETIC PEPTIDE
L40           3 SEA FILE=WPIX ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5) AND
                L6
L76         472 SEA FILE=WPIX ABB=ON  PLU=ON  NATRIURET? (1A) PEPTIDE
L77     1575921 SEA FILE=WPIX ABB=ON  PLU=ON  MEASUR? OR TEST? OR ASSAY? OR
                ANALY? OR IDENTIF?
L78          48 SEA FILE=WPIX ABB=ON  PLU=ON  L76 (10A) L77
L83        6177 SEA FILE=WPIX ABB=ON  PLU=ON  LIGAND (3A) BIND?
L84           8 SEA FILE=WPIX ABB=ON  PLU=ON  L78 AND L83
L85           5 SEA FILE=WPIX ABB=ON  PLU=ON  L84 NOT L40
```

```
L76         472 SEA FILE=WPIX ABB=ON  PLU=ON  NATRIURET? (1A) PEPTIDE
L77     1575921 SEA FILE=WPIX ABB=ON  PLU=ON  MEASUR? OR TEST? OR ASSAY? OR
                ANALY? OR IDENTIF?
L78          48 SEA FILE=WPIX ABB=ON  PLU=ON  L76 (10A) L77
L86      394854 SEA FILE=WPIX ABB=ON  PLU=ON  STABLE? OR STABILIZ?
L87           6 SEA FILE=WPIX ABB=ON  PLU=ON  L78 AND L86
```

```
=> s (l82 or l85 or l87) not l40
L92           8 (L82 OR L85 OR L87) NOT L40

=> dup rem l69 l89 l90 l91 l92
FILE 'MEDLINE' ENTERED AT 13:23:53 ON 14 SEP 2006

FILE 'CAPLUS' ENTERED AT 13:23:53 ON 14 SEP 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 13:23:53 ON 14 SEP 2006
Copyright (c) 2006 The Thomson Corporation

FILE 'EMBASE' ENTERED AT 13:23:53 ON 14 SEP 2006
Copyright (c) 2006 Elsevier B.V. All rights reserved.

FILE 'WPIX' ENTERED AT 13:23:53 ON 14 SEP 2006
COPYRIGHT (C) 2006 THE THOMSON CORPORATION
PROCESSING COMPLETED FOR L69
PROCESSING COMPLETED FOR L89
PROCESSING COMPLETED FOR L90
PROCESSING COMPLETED FOR L91
PROCESSING COMPLETED FOR L92
L93          37 DUP REM L69 L89 L90 L91 L92 (5 DUPLICATES REMOVED)
                ANSWER '1' FROM FILE MEDLINE
                ANSWERS '2-5' FROM FILE CAPLUS
                ANSWERS '6-24' FROM FILE BIOSIS
                ANSWERS '25-30' FROM FILE EMBASE
                ANSWERS '31-37' FROM FILE WPIX

=> d ibib ed abs l93 1-30; d ibib ab abex l93 31-37

L93  ANSWER 1 OF 37     MEDLINE on STN                    DUPLICATE 5
ACCESSION NUMBER:   90291671     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 2141557
TITLE:              Immunoradiometric assay of atrial natriuretic peptide in
                    unextracted plasma.
AUTHOR:             Tattersall J E; Dawnay A; McLean C; Cattell W R
CORPORATE SOURCE:   Department of Nephrology, St. Bartholomew's Hospital,
                    London, U.K.
SOURCE:             Clinical chemistry, (1990 Jun) Vol. 36, No. 6, pp. 855-9.
                    Journal code: 9421549. ISSN: 0009-9147.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        199007
ENTRY DATE:         Entered STN: 7 Sep 1990
                    Last Updated on STN: 7 Sep 1990
                    Entered Medline: 31 Jul 1990
ED   Entered STN: 7 Sep 1990
     Last Updated on STN: 7 Sep 1990
     Entered Medline: 31 Jul 1990
AB   We have developed and validated a two-site liquid-phase
     immunoradiometric assay (IRMA) of atrial natriuretic peptide
     (ANP) in unextracted human plasma. Both radiolabeled rabbit anti-ANP IgG
     and polyclonal mouse anti-ANP must bind to ANP for detection, and the
     assay is specific for peptides with both an intact C-terminus and a
```

disulfide bridge. The assay sensitivity (detection limit) is 0.96 pmol/L, and the working range is 2.3-300 pmol/L, with the hook effect occurring above 500 pmol/L. Results for diluted plasma from normal subjects and from patients with renal failure paralleled the standard curve; analytical recovery of ANP added to such samples averaged 94%. The between- and within-assay CVs at 8 pmol/L were 10% and 5%, respectively. The assay is sufficiently sensitive and precise to detect the postural change in ANP concentrations in normal subjects.

L93 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 1999:299573 CAPLUS
DOCUMENT NUMBER: 130:292093
TITLE: A **method** for suppressing the decomposition of natriuretic peptides and an improved assay of natriuretic peptides using this **method.**
INVENTOR(S): Shimizu, Hiroyuki; Asada, Hidehisa; Endo, Kazuaki
PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9922235	A1	19990506	WO 1998-JP1470	19980331
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2306751	AA	19990506	CA 1998-2306751	19980331
AU 9865208	A1	19990517	AU 1998-65208	19980331
AU 751660	B2	20020822		
EP 1030177	A1	20000823	EP 1998-911128	19980331
EP 1030177	B1	20050622		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 3302376	B2	20020715	JP 1999-523656	19980331
AT 298423	E	20050715	AT 1998-911128	19980331
ES 2244052	T3	20051201	ES 1998-911128	19980331
PRIORITY APPLN. INFO.:			JP 1997-292982 A	19971024
			WO 1998-JP1470 W	19980331

ED Entered STN: 17 May 1999
AB A method is described for suppressing the decomposition of mammalian natriuretic peptides, in particular, BNP by using containers wherein the surface contacting with samples is made of the material capable of suppressing the activation of a peptide-decomposing substance (e.g. proteinase). By this method, samples for assaying natriuretic peptides can be conveniently collected in a stable condition. Also, a reliable method is provided for assaying natriuretic peptides using these containers.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L93 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:259646 CAPLUS
DOCUMENT NUMBER: 142:291408
TITLE: **Method** of treating obesity and metabolic disorders related to excess adipose tissue by administration of natriuretic peptide receptor c inhibitors
INVENTOR(S): Chada, Kiran K.; Chouinard, Roland; Ashar, Hena; Sayed, Abu
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 768,566.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2005065092	A1	20050324	US 2004-898490		20040722
US 2004259789	A1	20041223	US 2004-768566		20040129
PRIORITY APPLN. INFO.:			US 2002-398785P	P	20020729
			US 2003-478206P	P	20030612
			US 2003-630423	A1	20030729
			US 2004-768566	A2	20040129

ED Entered STN: 25 Mar 2005
AB Disclosed is a method of using synthetic analogs of natriuretic peptides and more particularly to synthetic linear peptide analogs as pro-lipolytic, as anti-obesity agents, and as intermediates for or modulators of such useful compds. Inhibitors to nprC are disclosed to treat or prevent adipose accumulation in mammals.

L93 ANSWER 4 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:17398 CAPLUS
DOCUMENT NUMBER: 140:71527
TITLE: **Methods** and compositions for the stabilization of brain natriuretic peptide (BNP) in blood samples using proteinase inhibitors
INVENTOR(S): Belensky, Alexander; Bluestein, Barry
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 1378242	A1	20040107	EP 2003-13792		20030618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
CA 2430889	AA	20031219	CA 2003-2430889		20030603
AU 2003204649	A1	20040115	AU 2003-204649		20030612
JP 2004029021	A2	20040129	JP 2003-175441		20030619
US 2004067889	A1	20040408	US 2003-465691		20030619
PRIORITY APPLN. INFO.:			US 2002-389991P	P	20020619

ED Entered STN: 09 Jan 2004
AB The present invention describes methods and compns. comprising new protease inhibitor stabilizers of brain natriuretic peptide (BNP), which

prevent or significantly reduce the degradation of BNP in blood based samples, particularly plasma samples. The BNP inhibitors of the invention include D-Phe-Phe-Arg-chloromethylketone (PPACK), D-Phe-Pro-Arg-chloromethylketone (PPACK), acetyl-Leu-Leu-arginal (leupeptin), N-(Nα-carbonyl-Arg-Val-Arg-al)Phe (antipain) and diisopropylfluorophosphate (DFP), either alone or in combination. The inhibitors, and combinations thereof, can be directly added to collected blood samples prior to testing in laboratory or clin. settings. In addition, the inhibitors, alone or in combination, can be added to blood-based (e.g., plasma) matrixes prior to, or at the time of, the addition of exogenous BNP (e.g., synthetic BNP), to prepare control materials used in BNP anal. and quantification of patient blood samples.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L93 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:405438 CAPLUS
DOCUMENT NUMBER: 121:5438
TITLE: Eel ventricular **natriuretic peptide** : **isolation** of a low molecular size form and characterization of plasma form by homologous radioimmunoassay
AUTHOR(S): Takei, Y.; Takahashi, A.; Watanabe, T. X.; Nakajima, K.; Ando, K.
CORPORATE SOURCE: Ocean Res. Inst., Univ. Tokyo, Nakano, 164, Japan
SOURCE: Journal of Endocrinology (1994), 141(1), 81-9
CODEN: JOENAK; ISSN: 0022-0795
DOCUMENT TYPE: Journal
LANGUAGE: English
ED Entered STN: 09 Jul 1994
AB Ventricular **natriuretic peptide** (VNP) with 25 amino acid residues was isolated from the low mol. weight fraction of acid exts. of eel cardiac ventricles. No other short forms of VNP were recovered from the fraction. This peptide was named eel VNP(1-25) because it was a C-terminally truncated form of the previously isolated eel VNP(1-36). As observed before with eel VNP(1-36), eel VNP(1-25) had a much higher (146-fold) vasodepressor activity than human atrial **natriuretic peptide** (ANP) in eels, but was a third to a half as active in rats with respect to vasodepressor and natriuretic activities. Eel VNP(1-25) was generally less potent than eel VNP(1-36) for vasodepressor and natriuretic effects. A specific RIA has been developed for the measurement of eel VNP. The antiserum, raised against eel VNP(1-36), was highly specific and did not exhibit significant cross-reactivity with eel ANP and C-type **natriuretic peptide**, even though their amino acid sequences have more than 60% homol. with that of eel VNP. The sensitivity of assay was 0.5 fmol/tube for eel VNP(1-36) with more than 99% confidence. Such high sensitivity permitted direct assaying of VNP with only a few microliters of plasma. In fresh water eels, the concentration of VNP in the cardiac ventricle was higher than those in the atrium or brain and that of ANP in the ventricle. Thus, VNP seems to be a ventricular hormone. Although ANP is a major circulating hormone in mammals, the plasma concentration of VNP was threefold higher than that of ANP. The RIA coupled with gel-permeation chromatog. revealed that a 14 kDa form, probably proVNP, and smaller forms (3-6 kDa) circulate in eel plasma. Reverse-phase high performance **liquid** chromatog. **identified** both VNP(1-36) and VNP(1-25) in eel plasma; VNP(1-36) appeared to be a major form.

L93 ANSWER 6 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 2

ACCESSION NUMBER: 1999:487467 BIOSIS
DOCUMENT NUMBER: PREV199900487467
TITLE: Assessment of the **stability** of N-terminal pro-brain **natriuretic peptide** in vitro: Implications for assessment of left ventricular dysfunction.
AUTHOR(S): Downie, P. F.; Talwar, S.; Squire, I. B.; Davies, J. E.; Barnett, D. B.; Ng, L. L. [Reprint author]
CORPORATE SOURCE: Department of Medicine and Therapeutics, University of Leicester, Leicester Royal Infirmary, Robert Kilpatrick Clinical Sciences Building, Leicester, LE2 7LX, UK
SOURCE: Clinical Science (London), (Sept., 1999) Vol. 97, No. 3, pp. 255-258. print.
CODEN: CSCIAE. ISSN: 0143-5221.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 1999
Last Updated on STN: 16 Nov 1999
ED Entered STN: 16 Nov 1999
Last Updated on STN: 16 Nov 1999
AB Plasma concentrations of N-terminal pro-brain natriuretic peptide (NT-proBNP) are raised in patients with left ventricular dysfunction. **Measurement** of this peptide has a potential diagnostic role in the identification and assessment of patients with heart failure. The stability of this peptide over time periods and conditions pertaining to routine clinical practice has not been reported previously. Blood samples were obtained from 15 subjects. One aliquot was processed immediately, and the remaining portions of the blood samples were stored for 24 h or 48 h at room temperature or on ice prior to processing. Plasma concentrations of NT-proBNP were **measured** with a novel immunoluminometric **assay** developed within our laboratory. Mean plasma concentrations of NT-proBNP were not significantly different whether blood samples were centrifuged immediately and stored at -70 degreeC or kept at room temperature or on ice for 24 h or 48 h. The mean percentage differences from baseline (reference standard) were +5.2% (95% confidence interval +18.2 to -7.8%) and +0.8% (+15.2 to -13.7%) after storage for 24 h at room temperature or on ice respectively, and +8.9% (+24.2 to -6.5%) and +3.2% (+15.1 to -0.9%) for storage for 48 h at room temperature or on ice respectively. Pearson correlation coefficients for baseline NT-proBNP concentrations compared with levels at 48 h at room temperature or on ice were r = 0.89 and r = 0.83 respectively (both P < 0.0001). Thus NT-proBNP extracted from plasma samples treated with EDTA and aprotinin is stable under conditions relevant to clinical practice.

L93 ANSWER 7 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 3
ACCESSION NUMBER: 1998:444549 BIOSIS
DOCUMENT NUMBER: PREV199800444549
TITLE: Prolonged **stability** of brain **natriuretic peptide**: Importance for non-invasive assessment of cardiac function in **clinical** practice.
AUTHOR(S): Buckley, Martin G. [Reprint author]; Marcus, Neil J.; Yacoub, Magdi H.; Singer, Donald R. J.
CORPORATE SOURCE: Heart Sci. Cent., Natl. Heart and Lung Inst., Imperial Coll. Sch. Med., Harefield UB9 6LH, Middlesex, UK
SOURCE: Clinical Science (London), (Sept., 1998) Vol. 95, No. 3, pp. 235-239. print.
CODEN: CSCIAE. ISSN: 0143-5221.
DOCUMENT TYPE: Article
LANGUAGE: English

ENTRY DATE: Entered STN: 21 Oct 1998
Last Updated on STN: 21 Oct 1998
ED Entered STN: 21 Oct 1998
Last Updated on STN: 21 Oct 1998
AB 1. BNP and ANP are important research indices of severity of heart failure. However, uncertainty regarding the stability of these peptides at room temperature has limited their use to assess cardiac function in routine clinical practice. 2. We assessed the stability of BNP and ANP in blood samples left for 2 h or 2 days at room temperature compared with levels in blood processed immediately (initial). These times were chosen to reflect possible times for samples to be processed in a hospital outpatient clinic (2 h) or a blood sample posted to a laboratory from general practice (2 days). Samples were obtained from eight heart transplant recipients. Blood was separated and plasma storated immediately after collection (initial) and after 2 h or 2 days at room temperature respectively. 3. Initial, plasma-BNP and ANP values. **measured** by radioimmunoassay after Sep-Pak extraction were 38.9+-11.1 (S.E.M.) pg/ml and 113.6+-28.1 pg/ml, respectively. After 2 h at room temperature there was no significant fall in either peptide level (35.5+-9.9 pg/ml, BNP; 104.9+-30.6 pg/ml, ANP). However, after 2 days at room temperature there was a significant fall in ANP to 38.1+-12.6 pg/ml ($P<0.005$ versus initial level). In contrast, there was no significant fall in BNP after 2 days (32.0+-8.4 pg/ml). After 2 days at room temperature only 30.4+-4.3% of the ANP remained, but 86.0+-5.0% of BNP compared with the initial ANP and BNP **measurements.** 4. Our study clearly showed that ANP is stable for 2 h and thus could be useful as a screening **test** for heart disease in hospital. In contrast, BNP remained stable for 2 days. **Measuring** BNP may thus be practical as a **test** of heart function both for routine use in hospital and by general practitioners in the community.

L93 ANSWER 8 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 4
ACCESSION NUMBER: 1998:72640 BIOSIS
DOCUMENT NUMBER: PREV199800072640
TITLE: Brain **natriuretic peptide** is **stable** in whole blood and can be **measured** using a simple rapid **assay**: Implications for **clinical** practice.
AUTHOR(S): Murdoch, David R. [Reprint author]; Byrne, John; Morton, James J.; McDonagh, Theresa A.; Robb, Stephem D.; Clements, Suzanne; Ford, Ian; McMurray, John J. V.; Dargie, Henry J.
CORPORATE SOURCE: MRC Clinical Research Initiative Heart Failure, West Med. Building, Univ. Glasgow, Glasgow G12 8QQ, UK
SOURCE: Heart (London), (Dec., 1997) Vol. 78, No. 6, pp. 594-597. print.
ISSN: 1355-6037.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Feb 1998
Last Updated on STN: 24 Feb 1998
ED Entered STN: 24 Feb 1998
Last Updated on STN: 24 Feb 1998
AB Objectives-To compare the **stability** of brain **natriuretic peptide** (BNP) to that of N-terminal atrial **natriuretic peptide** (NT-ANP) in whole blood and plasma stored under different conditions. To compare a rapid, simple, direct (unextracted) BNP **assay** to a conventional **assay** using plasma extraction. Design-Blinded, prospective, comparative study. Setting-Tertiary referral cardiology department. Subjects-Forty two subjects (24 men, 18 women)

comprising 28 patients with left ventricular systolic dysfunction (LVSD) ranging from mild to severe and 14 healthy volunteers. Main outcome **measures**-Stability of NT-ANP and BNP when stored as whole blood or plasma at room temperature over three days. Reproducibility of **measurements.** Results-BNP was stable in whole blood stored at room temperature for three days; mean change in concentration -7.4% (95% CI 0.6 to -14.8), (direct), -6.3% (5.0 to -16.4), (extracted); whereas a significant decline in BNP concentration was noted in plasma stored at room temperature; -23.2% (-13.7 to -31.6), (direct); -14.4% (-3.2 to -24.3), (extracted). By contrast a small nonsignificant rise in NT-ANP concentration was noted both in whole blood and plasma stored at room temperature for three days; whole blood +8.6% (+22.3 to -3.5), plasma +6.3%, (23.2 to -8.4). The reproducibility of the BNP **measurements**, and particularly the rapid, direct, **measurement**, was superior to that for NT-ANP. Conclusions-BNP is shown to be stable in whole blood for three days and can be **measured** using a rapid, simple **assay.** Routine **assay** of BNP is feasible in ordinary clinical practice and may be of value to general practitioners and hospital based physicians in the diagnosis and management of patients with LVSD. Samples can be sent to a central laboratory without special handling requirements.

L93 ANSWER 9 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:90338 BIOSIS
DOCUMENT NUMBER: PREV200600089521
TITLE: The effects of **sucrose** on **stability** of human brain **natriuretic peptide** [hBNP (1-32)] and human parathyroid hormone [hPTH (1-34)].
AUTHOR(S): Kamberi, M. [Reprint Author]; Kim, Y. J.; Jun, B.; Riley, C. M.
CORPORATE SOURCE: 1501 Calif Ave, Palo Alto, CA 94304 USA
kmarika55@hotmail.com
SOURCE: Journal of Peptide Research, (DEC 2005) Vol. 66, No. 6, pp. 348-356.
ISSN: 1397-002X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Jan 2006
Last Updated on STN: 25 Jan 2006
ED Entered STN: 25 Jan 2006
Last Updated on STN: 25 Jan 2006
AB Although the effect of sucrose on the physical stability of proteins has been well documented, its impact on their chemical stability is largely unknown. The aim of this study was to investigate the potential effects of sucrose on the structural conformation of human brain natriuretic peptide [hBNP (1-32)] and the synthetic human parathyroid hormone [hPTH (1-34)], and link these effects to chemical degradation pathways of these peptides. The stability of hBNP (1-32) and hPTH (1-34) was studied at pH 5.5. Aggregation was monitored using size exclusion high-performance liquid chromatography (SE-HPLC), whereas oxidation and deamidation products were **measured** by reversed phase (RP) HPLC. Fourier transform infrared (FT-IR) spectroscopy was used to study the peptides' conformation. Sucrose retarded aggregation, deamidation, and oxidation of hBNP (1-32) and hPTH (1-34), with a maximum effect at relatively high concentrations (as much as 1 m). FT-IR spectroscopy indicated that sucrose maintained the native conformation of hBNP (1-32) and induced small conformation changes in the hPTH (1-34) structure. Sucrose enhanced the stability of hBNP (1-32) and hPTH (1-34) in liquid formulations. The stabilizing effect of sucrose was due to a large extent to retardation of oxidation and deamidation of hBNP (1-32) and hPTH (1-34).

L93 ANSWER 10 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:13095 BIOSIS
DOCUMENT NUMBER: PREV200600015683
TITLE: **Stability** of B-type **natriuretic peptide** (BNP) in whole blood and plasma stored under different conditions.
AUTHOR(S): Azzazy, H. M. [Reprint Author]; Duh, S.; Antwi, S.; Christenson, R. H.
CORPORATE SOURCE: Univ Maryland, Sch Med, Baltimore, MD 21201 USA
SOURCE: Clinical Chemistry, (2005) Vol. 51, No. Suppl. 6, pp. A27. Meeting Info.: Annual Meeting of the American-Association-for-Clinical-Chemistry. Orlando, FL, USA. July 24 -28, 2005. Amer Assoc Clin Chem.
CODEN: CLCHAU. ISSN: 0009-9147.
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Dec 2005
Last Updated on STN: 21 Dec 2005
ED Entered STN: 21 Dec 2005
Last Updated on STN: 21 Dec 2005

L93 ANSWER 11 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:510695 BIOSIS
DOCUMENT NUMBER: PREV200510309665
TITLE: **Clinical** and laboratory diagnostics of cardiovascular disease: Focus on natriuretic peptides and cardiac ischemia.
AUTHOR(S): Omland, Torbjorn [Reprint Author]
CORPORATE SOURCE: Univ Oslo, Fac Div, Akershus Univ Hosp, Dept Med, NO-1474 Nordbyhagen, Norway
torbjorn.omland@medisin.uio.no
SOURCE: Scandinavian Journal of Clinical and Laboratory Investigation, (2005) Vol. 65, No. Suppl. 240, pp. 18-24.
CODEN: SJCLAY. ISSN: 0036-5513.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Nov 2005
Last Updated on STN: 23 Nov 2005
ED Entered STN: 23 Nov 2005
Last Updated on STN: 23 Nov 2005
AB Chest pain is the most common clinical presentation of acute ischemic heart disease, but only one third of these patients are ultimately found to have an acute coronary syndrome. Initial assessment of the patient presenting with chest pain includes a careful history, physical examination, an initial electrocardiogram (ECG) and **measurement** of biochemical markers of myocardial injury. The **natriuretic peptide** system is activated in a broad spectrum of cardiovascular diseases, including acute coronary syndromes and **stable** coronary disease. A strong relation between plasma levels of B-type natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) obtained in the subacute phase, and long-term, all-cause mortality, as well as the rate of re-admissions for heart failure after myocardial infarction, has been documented. Persistently elevated NT-proBNP levels during the first 72 hours following admission for an acute coronary syndrome have recently been associated with the presence of refractory ischemia and high risk of short-term recurrent ischemic events. Patients with signs of

exercise-induced ischemia by dobutamine stress echocardiography have been reported to have higher baseline BNP values. Moreover, BNP and NT-proBNP levels are increased acutely in proportion to the magnitude of the inducible perfusion defect observed during stress **testing**, suggesting that BNP and NT-proBNP are markers of acute ischemia. Recently, a relationship between circulating levels of BNP and NT-proBNP and long-term all cause mortality in patients with stable coronary artery disease has been documented.

L93 ANSWER 12 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2005:302253 BIOSIS
DOCUMENT NUMBER: PREV200510087800
TITLE: High intraindividual variation of B-type **natriuretic peptide** (BNP) and amino-terminal **proBNP** in patients with **stable** chronic heart failure.
AUTHOR(S): Bruins, Sanne; Fokkema, Rebecca [Reprint Author]; Romer, Jeroen W. P.; DeJongste, Mike J. L.; Van der Dijs, Fey P. L.; Van den Ouweland, Jody M. W.; Muskiet, Frits A. J.
CORPORATE SOURCE: Univ Groningen Hosp, Dept Cardiol, CMCV, Room Y1-165,POB 30-001, NL-9700 RB Groningen, Netherlands
SOURCE: Clinical Chemistry, (NOV 2004) Vol. 50, No. 11, pp. 2052-2058.
CODEN: CLCHAU. ISSN: 0009-9147.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Aug 2005
Last Updated on STN: 15 Aug 2005
ED Entered STN: 15 Aug 2005
Last Updated on STN: 15 Aug 2005

AB Background: Plasma B-type natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP) are promising markers for heart failure diagnosis, prognosis, and treatment. Insufficient data on the intraindividual biological variation (CVi) of BNP and NT-proBNP hamper interpretation of changes in concentration on disease progression or treatment optimization. We therefore investigated CVi values in stable heart failure patients.Methods: We recruited 43 patients with stable chronic heart failure living in Curacao (22 males, 21 females; median age, 63 years; range, 20-86 years; New York Heart Association classes I-III). Samples were collected for within-day CVi (n = 6; every 2 h starting at 0800), day-to-day CVi (n = 5; samples collected between 0800 and 1000 on 5 consecutive days), and week-to-week CVi (n = 6; samples collected between 0800 and 1000 on the same day of the week for 6 consecutive weeks). NT-proBNP (Roche) and BNP (Abbott) were **measured** by immunoassay.Results: Median (range) concentrations were 134 (01630) ng/L (BNP) and 570 (17-5048) ng/L (NT-proBNP). **Analytical** variation, week-to-week CVi, and reference change values were 8.4%, 40%, and 113% (BNP), and 3.0%, 35%, and 98% (NT-proBNP). Week-to week CV(i)s were inversely related to median BNP concentrations. Week-to week CVis for BNP were 44% (BNP less than or equal to350 ng/L) and 30% (BNP >350 ng/L). Both BNP and NT-proBNP increased between 0800 and 1000. Median NT-proBNP/BNP ratios were inversely related to median BNP concentrations.Conclusions: The high CV(i)s hamper interpretation of changes in BNP and NT-proBNP concentrations and may partly explain their poor diagnostic values in chronic heart failure. Easily modifiable determinants to lower CVi have not been identified. The value of BNP and NT-proBNP for chronic heart failure diagnosis, and especially for follow-up and treatment optimization of individuals, remains largely to be established. (C) 2004 American Association for Clinical Chemistry.

L93 ANSWER 13 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:433696 BIOSIS
DOCUMENT NUMBER: PREV200400431601
TITLE: Long-term **stability** of endogenous B-type **natriuretic peptide** (BNP) and amino terminal **proBNP** (NTproBNP) in frozen plasma samples.
AUTHOR(S): Mueller, Thomas; Gegenhuber, Alfons; Dieplinger, Benjamin; Poelz, Werner; Haltmayer, Meinhard [Reprint Author]
CORPORATE SOURCE: Dept Lab Med, Koventhosp Barmherzige Brueder, Seilerstaette 2, A-4021, Linz, Austria
meinhard.haltmayer@bblinz.at
SOURCE: Clinical Chemistry and Laboratory Medicine, (2004) Vol. 42, No. 8, pp. 942-944. print.
ISSN: 1434-6621.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Nov 2004
Last Updated on STN: 10 Nov 2004
ED Entered STN: 10 Nov 2004
Last Updated on STN: 10 Nov 2004
AB The aim of the present study was to assess the longterm **stability** of endogenous Btype **natriuretic peptide** (BNP) and amino terminal proBNP (NTproBNP) in plasma samples stored at -20degreeC without addition of protease inhibitors (e.g., aprotinin). Stability of BNP and NTproBNP was **tested** in 60 EDTA plasma samples with BNP values between 30 and 420 pg/ml. Initial BNP and NTproBNP plasma concentrations were determined within four hours after blood collection using the AxSYM BNP and the Elecsys NTproBNP **assays.** Subsequently, all samples were stored at -20degreeC and were thawed for the second BNP and NTproBNP determination on the two instruments after one day, 30 days, 60 days, 90 days and 120 days, respectively. Mean recovery (i.e., residual immunoreactivity) of BNP and NTproBNP expressed in percent of the initial value for the given time interval of storage was calculated. Mean recovery of BNP was less than 70% after one day of storage at -20degreeC and decreased to less than 50% after two to four months of storage (e.g., recovery of endogenous BNP after three months of storage at -20degreeC ranging from 0% to 71%). In contrast, mean recovery of NTproBNP was generally greater than 90%, irrespective of the duration of storage at -20degreeC (e.g., recovery of endogenous NTproBNP after three months of storage at -20degreeC ranging from 91% to 112%). In conclusion, the determination of endogenous BNP with the AxSYM **assay** using frozen plasma samples may not be valid under the conditions **tested.** In contrast, NTproBNP as **measured** by the Elecsys **assay** may be stored at -20degreeC for at least four months without a relevant loss of the immunoreactive **analyte** .

L93 ANSWER 14 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2004:155886 BIOSIS
DOCUMENT NUMBER: PREV200400156570
TITLE: The effect of class-specific protease inhibitors on the **stabilization** of B-type **natriuretic peptide** in human plasma.
AUTHOR(S): Belenky, Alexander [Reprint Author]; Smith, Andrew; Zhang, Bin; Lin, Spencer; Despres, Normand; Wu, Alan H. B.; Bluestein, Barry I.

CORPORATE SOURCE: Diagnostics Division, Laboratory Testing Segment, Research and Development, Bayer Healthcare LLC, 511 Benedict Avenue, Tarrytown, NY, 10591, USA
alexander.belenky.b@bayer.com
SOURCE: Clinica Chimica Acta, (February 2004) Vol. 340, No. 1-2, pp. 163-172. print.
ISSN: 0009-8981 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004
ED Entered STN: 17 Mar 2004
Last Updated on STN: 17 Mar 2004
AB Background: B-type natriuretic peptide (BNP) is a cardiac hormone that regulates hemodynamic equilibrium. In the circulation, its activity is controlled by proteolytic factors. Accurate **measurement** of BNP in a patient's plasma may be affected by degradation due to proteolysis. Objective: We report on the identification and performance of classes of protease inhibitors that stabilize BNP in plasma. Design and methods: Using the Bayer ADVIA Centaur(R) BNP **assay**, we **measured** the effect of arginine, serine and/or specific kallikrein protease inhibitors (PIs) on exogenous spiked or endogenous BNP in patient plasma. Results: Compared to controls without inhibitor, all PIs were capable, to varying degrees, of retarding the rate of proteolytic degradation. The kallikrein-specific inhibitor, D-Phe-Phe-Arg-chloromethylketone (PPACK II) was most effective as a single constituent and was able to eliminate BNP degradation in patient samples for up to 6-10 days when stored at 2-8 degreeC. Conclusions: The stability of BNP was markedly increased in the presence of kallikrein-specific PPACK II and a broad spectrum of serine PIs. Use of these compounds offers a simple method of extending sample handling and storage of plasma samples containing BNP.

L93 ANSWER 15 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:372344 BIOSIS
DOCUMENT NUMBER: PREV200300372344
TITLE: N-Terminal pro-brain **natriuretic peptide** (**proBNP**) technical performance and **analyte stability** evaluation on the Roche Diagnostics Elecsys(R) immunoassay platform.
AUTHOR(S): Nowatzke, W. L. [Reprint Author]; Sokoll, L. J.; Chen, D. W.; Cole, T. G. [Reprint Author]; McKenna, M. L. [Reprint Author]; Bruzek, D. J.; Foster, A. P.
CORPORATE SOURCE: Washington University School of Medicine, St. Louis, MO, USA
SOURCE: Clinical Chemistry, (June 2003) Vol. 49, No. S6, pp. A61. print.
Meeting Info.: 55th Annual Meeting of the AACC (American Association for Clinical Chemistry). Philadelphia, PA, USA. July 20-24, 2003. American Association for Clinical Chemistry.
CODEN: CLCHAU. ISSN: 0009-9147.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Aug 2003
Last Updated on STN: 13 Aug 2003
ED Entered STN: 13 Aug 2003
Last Updated on STN: 13 Aug 2003

L93 ANSWER 16 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:235864 BIOSIS
DOCUMENT NUMBER: PREV200200235864
TITLE: **Stability** of B-type **natriuretic peptide** levels during exercise in patients with congestive heart failure: Implications for outpatient monitoring with B-type natriuretic peptide.
AUTHOR(S): McNairy, Matthew; Gardetto, Nancy; Clopton, Paul; Garcia, Alex; Krishnaswamy, Padma; Kazanegra, Radmila; Ziegler, Michael; Maisel, Alan S. [Reprint author]
CORPORATE SOURCE: VAMC Cardiology, 3350 La Jolla Village Drive, 111-A, San Diego, CA, 92161, USA
amaisel@ucsd.edu
SOURCE: American Heart Journal, (March, 2002) Vol. 143, No. 3, pp. 406-411. print.
CODEN: AHJOA2. ISSN: 0002-8703.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Apr 2002
Last Updated on STN: 10 Apr 2002
ED Entered STN: 10 Apr 2002
Last Updated on STN: 10 Apr 2002

AB Background B-natriuretic peptide (BNP), a neurohormone secreted from the cardiac ventricles, reflects left ventricular pressure and correlates to disease severity and prognosis. The fact that BNP levels can now be **measured** by a rapid **assay** suggests its potential usefulness in the outpatient clinic. However, if patient activity were to markedly alter BNP levels, its use would be less attractive for monitoring patients in the outpatient clinical setting. Methods A total of 30 patients (10 normal, 10 New York Heart Association (NYHA) class I-II, 10 NYHA class III-IV) exercised with an upright bicycle protocol. Exercise was carried out to 75% of maximum heart rate, and venous blood was sampled before, immediately after, and 1 hour after completion of exercise. Plasma levels of BNP, epinephrine, and norepinephrine were **measured.** Results BNP levels at baseline were 29 +- 11 pg/mL for normal subjects, 126 +- 26 pg/mL for NYHA I-II subjects, and 1712 +- 356 pg/mL for NYHA III-IV subjects. The change in BNP levels with exercise was significantly lower than the change in epinephrine and norepinephrine ($P < .001$). In normal subjects, BNP increased from 29 pg/mL to 44 pg/mL with peak exercise, still within the range of normal (< 100 pg/mL). This is compared with larger increases of norepinephrine (716 pg/mL to 1278 pg/mL) and epinephrine (52 pg/mL to 86 pg/mL) with exercise in normal subjects. There were also only small increases in BNP with exercise in patients with congestive heart failure (NYHA I-II, 30%; NYHA III-IV, 18%). For the same groups, epinephrine levels increased by 218% and 312%, respectively, and norepinephrine levels increased by 232% and 163%, respectively. One hour after completion of exercise, there were only minimal changes in BNP levels from baseline state in normal subjects (+0.9%) and patients with NYHA I-II (3.8%). In patients with NYHA III-IV, there was a 15% increase from baseline 1 hour after exercise. Conclusions BNP levels show only minor changes with vigorous exercise, making it unlikely that a normal patient would be classified as having congestive heart failure based on a BNP level obtained after activity. Prior activity should not influence BNP levels in patients with congestive heart failure. Therefore, when a patient presents to clinic with a marked change in their BNP level, it may reflect a real change in their condition.

L93 ANSWER 17 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on

STN
ACCESSION NUMBER: 2001:452217 BIOSIS
DOCUMENT NUMBER: PREV200100452217
TITLE: Plasma A- and B-type natriuretic peptides: Physiology, methodology and **clinical** use.
AUTHOR(S): Boomsma, Frans [Reprint author]; van den Meiracker, Anton H.
CORPORATE SOURCE: Internal Medicine, University Hospital Dijkzigt, Dr. Molewaterplein 40, Rm L-276, 3015 GD, Rotterdam, Netherlands
boomsma@inw1.azr.nl
SOURCE: Cardiovascular Research, (15 August, 2001) Vol. 51, No. 3, pp. 442-449. print.
CODEN: CVREAU. ISSN: 0008-6363.
DOCUMENT TYPE: Article
General Review; (Literature Review)
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Sep 2001
Last Updated on STN: 22 Feb 2002
ED Entered STN: 26 Sep 2001
Last Updated on STN: 22 Feb 2002

L93 ANSWER 18 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:450644 BIOSIS
DOCUMENT NUMBER: PREV200000450644
TITLE: **Stability** of brain **natriuretic peptide** (BNP) in human whole blood and plasma.
AUTHOR(S): Gobinet-Georges, Agnes [Reprint author]; Valli, Nathalie; Filliatre, Helene; Dubernet, Marie-France; Dedeystere, Olivier; Bordenave, Laurence
CORPORATE SOURCE: Service de Medecine Nucleaire, Hopital du Haut-Leveque, CHU de Bordeaux, Avenue Magellan, F-33604, Pessac Cedex, France
SOURCE: Clinical Chemistry and Laboratory Medicine, (June, 2000) Vol. 38, No. 6, pp. 519-523. print.
ISSN: 1434-6621.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Oct 2000
Last Updated on STN: 10 Jan 2002
ED Entered STN: 25 Oct 2000
Last Updated on STN: 10 Jan 2002
AB Brain natriuretic peptide is proposed as a biochemical marker which could provide a useful screening **test** to select patients for further cardiac investigations in heart failure. The applicability of such a biochemical **test** in clinics, hospital wards, and clinical laboratories is dependent on its ease of use and on the complexity of sample handling. The present study was undertaken to evaluate the **stability** of brain **natriuretic peptide** under a number of different handling conditions (sample collection, storage temperatures, freezing temperatures) **assayed** with a commercially available kit. The results clearly demonstrate that brain **natriuretic peptide** is **stable** at room temperature for 24 hours, or in up to 30 degreeC for 12 hours in the presence and absence of aprotinin, on the condition that brain natriuretic peptide is **assayed** within one month (frozen at -20 degreeC) after blood collection. The presence of aprotinin prevents brain natriuretic peptide degradation in samples preserved for more than 1 month at -20 degreeC before **assay.**

L93 ANSWER 19 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:86315 BIOSIS
DOCUMENT NUMBER: PREV199900086315
TITLE: Expression and purification of the extracellular **ligand-binding** domain of the atrial natriuretic peptide (ANP) receptor: Monovalent binding with ANP induces 2:2 complexes.
AUTHOR(S): Misono, Kunio S. [Reprint author]; Sivasubramanian, Natarajan; Berkner, Kathleen; Zhang, Xiaolun
CORPORATE SOURCE: Dep. Molecular Cardiol., Lerner Res. Inst. Cleveland Clinic Foundation, 9500 Euclid Ave., Cleveland, OH 44195, USA
SOURCE: Biochemistry, (Jan. 12, 1999) Vol. 38, No. 2, pp. 516-523. print.
CODEN: BICHAW. ISSN: 0006-2960.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Mar 1999
Last Updated on STN: 1 Mar 1999
ED Entered STN: 1 Mar 1999
Last Updated on STN: 1 Mar 1999
AB The receptor for atrial natriuretic peptide (ANP) is a type-I transmembrane protein containing an extracellular **ligand-binding** domain, a single transmembrane sequence, an intracellular kinasehomologous domain, and a guanylate cyclase (GCase) domain. Binding of ANP to the extracellular domain causes activation of the GCase domain by an as yet unknown mechanism. To facilitate studies of the receptor structure and signaling mechanism, we have expressed the extracellular ANP-binding domain of rat ANP receptor (NPR-ECD) in a water-soluble form. NPR-ECD was purified to homogeneity by ANPaffinity chromatography. SDS-PAGE gave a single 61-kDa band, which coincided with a radioactive band obtained by photoaffinity-labeling with N4alpha-azidobenzoyl-125I-ANP(4-28). Edman degradation gave a single amino-terminal sequence expected for the mature protein. Both trifluoromethanesulfonic acid and peptide-N-glycosidase F treatments yielded a 50-kDa band, indicating N-glycosylation. The molecular mass of 57 725 Da determined by mass spectrometry indicates the carbohydrate content at 16%. NPR-ECD bound ANP with an affinity comparable to that of the full-length receptor. The ligand selectivity of NPR-ECD (in the order ANP > brain natriuretic peptide mchgt C-type natriuretic peptide) was also similar to that of the full-length receptor. HPLC gel filtration of NPR-ECD gave a peak with an apparent mass of 74 kDa. Preincubation with ANP generated a new 150-kDa peak with a concomitant decrease of the 74-kDa peak. This shift in peak positions was ANP concentration-dependent and was complete at the NPR-ECD-to-ANP molar ratio of 1: 1, indicating equimolar binding. The change in the apparent native molecular weight from 74 to 150 kDa suggests that binding causes dimerization of the NPR-ECD:ANP complex to yield an (NPR-ECD:ANP)2 complex.

L93 ANSWER 20 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:334449 BIOSIS
DOCUMENT NUMBER: PREV199900334449
TITLE: Development of a novel, N-Terminal-**proBNP** (NT-**proBNP**) **assay** with a low detection limit.
AUTHOR(S): Karl, J. [Reprint author]; Borgya, A.; Gallusser, A.; Huber, E.; Krueger, K.; Rollinger, W.; Schenk, J.
CORPORATE SOURCE: Roche Diagnostics GmbH, Tutzing, Germany
SOURCE: Scandinavian Journal of Clinical and Laboratory Investigation, (1999) Vol. 59, No. SUPPL. 230, pp. 177-181.

print.
CODEN: SJCLAY. ISSN: 0036-5513.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Aug 1999
Last Updated on STN: 24 Aug 1999
ED Entered STN: 24 Aug 1999
Last Updated on STN: 24 Aug 1999
AB A novel, highly sensitive and specific N-Terminal-proBNP (NT-proBNP) **assay** based on a sandwich format has been developed. The **assay** time is below 2 hours and no extraction process is needed. The calibration curve covers a NT-proBNP concentration range from 0 pmol/L up to 600 pmol/L. The **analytical** detection limit of the **assay** was estimated to be 2.7 pmol/L (3 SD). The intra-**assay** coefficient of variation is 5.7 % (at 50 pmol/L) and 6.1 % (at 250 pmol/L), while the inter-**assay** CVs are 15.8 % (15 pmol/L) and 8.2 % (250 pmol/L). There is no significant interference by bilirubin (up to 900 mumol/L), haemoglobin (up to 10 g/L), rheumatoid factors (up to 975 IU/mL), triglycerides (up to 20.5 mmol/L), biotin (up to 50 mug/L), digoxin (up to 100 mug/L) and digitoxin (up to 200 mug/L). The **analyte** NT-proBNP is fully stable in whole blood over 3 days and in EDTA-plasma over 24 hours. This good **stability** of NT-proBNP compared to other less **stable natriuretic peptides** is a significant advantage and a main prerequisite for a routine diagnostic marker. Preliminary results of using this new **assay** in clinical studies for diagnosing and monitoring left ventricular dysfunction demonstrate that there is a significant gain in diagnostic validity.

L93 ANSWER 21 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:429887 BIOSIS
DOCUMENT NUMBER: PREV199900429887
TITLE: **Stability** of brain **natriuretic peptide** (BNP) in human blood samples.
AUTHOR(S): Shimizu, Hiroyuki [Reprint author]; Aono, Kazuyoshi; Masuta, Keiichi; Asada, Hidehisa; Misaki, Atsushi; Teraoka, Hiroshi
CORPORATE SOURCE: Diagnostic Science Division, Shionogi and Co., Ltd., 2-5-1 Mishima, Settsu, Osaka, 566-0022, Japan
SOURCE: Clinica Chimica Acta, (July, 1999) Vol. 285, No. 1-2, pp. 169-172. print.
CODEN: CCATAR. ISSN: 0009-8981.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 18 Oct 1999
Last Updated on STN: 18 Oct 1999
ED Entered STN: 18 Oct 1999
Last Updated on STN: 18 Oct 1999
AB **Stability** of immunoreactivity of human brain **natriuretic peptide** (BNP) in blood samples was investigated. After storage of the whole blood samples in the blood collecting tubes made of glass or polyethylene terephthalate (PET), residual immunoreactivity of BNP in the plasma was **measured** by sandwich radioimmunoassay for human BNP. BNP in the blood samples collected in the PET tubes were kept more stable than that in the glass tubes. The results suggested that commercially available PET tubes would enable more accurate BNP values and this would also help to simplify the sample preparation.

L93 ANSWER 22 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on

STN
ACCESSION NUMBER: 1999:395208 BIOSIS
DOCUMENT NUMBER: PREV199900395208
TITLE: **Stability** of N-terminal pro-brain **natriuretic peptide** and brain **natriuretic peptide** in different sampling media and varying sample handling.
AUTHOR(S): Niederau, C. [Reprint author]; Fischer, Y. [Reprint author]; Stiegler, H. [Reprint author]; Kolbe-Busch, S. [Reprint author]; Haass, M.; Karl, J.; Schenk, J.; Reinauer, H. [Reprint author]
CORPORATE SOURCE: Department of Clinical Chemistry and Laboratory Diagnostics, Heinrich-Heine-University Medical Center, Duesseldorf, Germany
SOURCE: Clinical Chemistry, (June, 1999) Vol. 45, No. 6 PART 2, pp. A142. print.
Meeting Info.: 51st Annual Meeting of the American Association of Clinical Chemistry. New Orleans, Louisiana, USA. July 25-29, 1999. American Association of Clinical Chemistry.
CODEN: CLCHAU. ISSN: 0009-9147.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Oct 1999
Last Updated on STN: 8 Oct 1999
ED Entered STN: 8 Oct 1999
Last Updated on STN: 8 Oct 1999

L93 ANSWER 23 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1994:342059 BIOSIS
DOCUMENT NUMBER: PREV199497355059
TITLE: **Stability** of human atrial **natriuretic peptide** in blood samples.
AUTHOR(S): Tsuji, Tetsuo; Masuda, Hidesuke; Imagawa, Keiichdi; Haraikawa, Makoto; Shibata, Kazunori; Kono, Masao; Inouye, Ken [Reprint author]; Uchida, Kiyohisa
CORPORATE SOURCE: Res. Development Lab., Diagnostic Sci. Dep., Shionogi and Co. Ltd., 2-5-1 Mishima, Settsu-shi, Osaka 566, Japan
SOURCE: Clinica Chimica Acta, (1994) Vol. 225, No. 2, pp. 171-177.
CODEN: CCATAR. ISSN: 0009-8981.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Aug 1994
Last Updated on STN: 9 Aug 1994
ED Entered STN: 8 Aug 1994
Last Updated on STN: 9 Aug 1994

L93 ANSWER 24 OF 37 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1993:536733 BIOSIS
DOCUMENT NUMBER: PREV199345123827
TITLE: **Stability** of atrial **natriuretic peptide** under various **assay** conditions in normal and heart failure canine plasma.
AUTHOR(S): Heublein, Denise M.; Wei, Chi-Ming; Clavell, Alfredo L.; Burnett, John C., Jr.
CORPORATE SOURCE: Mayo Clinic Foundation, Rochester, MN, USA

SOURCE: Clinical Research, (1993) Vol. 41, No. 3, pp. 633A. Meeting Info.: Joint Meeting of the Central Society for Clinical Research, Midwest Section of the American Federation for Clinical Research and Central Region of the Society for Investigative Dermatology. Chicago, Illinois, USA. November 3-5, 1993. CODEN: CLREAS. ISSN: 0009-9279.
DOCUMENT TYPE: Conference; (Meeting)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Nov 1993 Last Updated on STN: 30 Nov 1993
ED Entered STN: 30 Nov 1993 Last Updated on STN: 30 Nov 1993

L93 ANSWER 25 OF 37 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004149906 EMBASE
TITLE: Effect of different sample types and **stability** after blood collection of N-terminal pro-B-type **natriuretic peptide** as **measured** with roche **elecsys** system [2].
AUTHOR: Van Der Merwe D.-E.; Henley R.; Lane G.; Field R.; Frenneaux M.; Dunstan F.; McDowell I.
CORPORATE SOURCE: D.-E. Van Der Merwe, Dept. of Med. Biochem. and Immunol., University Hospital of Wales, Univ. of Wales College of Medicine, Cardiff CF14 4XW, United Kingdom. DaElene.VanDerMerwe@CardiffandVale.wales.nhs.uk
SOURCE: Clinical Chemistry, (2004) Vol. 50, No. 4, pp. 779-780. . Refs: 7 ISSN: 0009-9147 CODEN: CLCHAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Letter
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry
LANGUAGE: English
ENTRY DATE: Entered STN: 29 Apr 2004 Last Updated on STN: 29 Apr 2004
ED Entered STN: 29 Apr 2004 Last Updated on STN: 29 Apr 2004
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L93 ANSWER 26 OF 37 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004512859 EMBASE
TITLE: Evaluation of N-terminal pro-B type natriuretic peptide analysis on the **Elecsys**.RTM. 1010 and 2010 analysers.
AUTHOR: Barnes S.C.; Collinson P.O.; Galasko G.; Lahiri A.; Senior R.
CORPORATE SOURCE: S.C. Barnes, Department of Chemical Pathology, St George's Hospital, London SE1 7EH, United Kingdom. sophie.barnes@gstt.nhs.uk
SOURCE: Annals of Clinical Biochemistry, (2004) Vol. 41, No. 6, pp. 459-463. . Refs: 5 ISSN: 0004-5632 CODEN: ACBOBU
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy

027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Dec 2004
Last Updated on STN: 17 Dec 2004
ED Entered STN: 17 Dec 2004
Last Updated on STN: 17 Dec 2004
AB Background: N-terminal pro-B type natriuretic peptide (NTpBNP) is a potential marker of cardiac failure. Methods: The Roche Elecsys® 1010 and 2010 **assays** for NTpBNP were evaluated for precision, sample **stability**, and correlation between sample types and with other **natriuretic peptides**. Samples from 290 individuals aged 45-89 years with no cardiovascular risk factors, renal failure, electrocardiogram changes, evidence of structural abnormalities, or wall motion abnormalities on echocardiography and with an ejection fraction >50% were used to provide reference NTpBNP ranges. Results: The intra-**assay** imprecision was <10% across the analytical range and <3% at all concentrations analysed >30 ng/L. Inter-**assay** imprecision was 5.3-6.7% on the Elecsys 1010 and 4.4-5.0% on the Elecsys 2010, in the range 380-13000 ng/L. There was no statistically significant change in NTpBNP following storage in whole-blood samples at room temperature for 24 h before centrifugation; serum samples at room temperature for 7 days, at 4 °C for up to 11 days on clot-activation gel or 22 days separated from the gel. NTpBNP concentrations were stable throughout five freeze-thaw cycles. There was a close correlation between NTpBNP concentrations in matched serum, EDTA plasma and lithium-heparin plasma samples. NTpBNP and BNP were more closely associated than were N-terminal proatrial natriuretic peptide and NTpBNP. This association was stronger at lower concentrations. NTpBNP concentrations increased with age, with values higher in women than men. Conclusions: NTpBNP is a stable molecule that can be **measured** easily and precisely using the Roche Elecsys 1010 or 2010 immunoassay analysers.

L93 ANSWER 27 OF 37 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004074684 EMBASE
TITLE: [Immunoradiometric **assay** of brain **natriuretic peptide** (BNP): Analytical and clinical study of the **assay kit** IRMA BNP Cis bio international].
DOSAGE IMMUNORADIOMETRIQUE DU PEPTIDE NATRIURETIQUE DE TYPE B (BNP): ETUDE ANALYTIQUE ET CLINIQUE DE LA TROUSSE IRMA BNP CIS BIO INTERNATIONAL.
AUTHOR: Mendes-Plogin A.; Georges A.; Valli N.; Dartiguelongue H.; Dubernet M.-F.; Bordenave L.
CORPORATE SOURCE: A. Mendes-Plogin, Medecine Nucleaire, Hop. du Haut-Leveque, Pessac, France. anne.plogin@chu-bordeaux.fr
SOURCE: Immuno-Analyse et Biologie Specialisee, (2002) Vol. 17, No. 5, pp. 336-340. .
Refs: 19
ISSN: 0923-2532 CODEN: IBSPEW
PUBLISHER IDENT.: S 0923-2532(02)01220-6
COUNTRY: France
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
029 Clinical Biochemistry
LANGUAGE: French

SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 4 Mar 2004
Last Updated on STN: 4 Mar 2004
ED Entered STN: 4 Mar 2004
Last Updated on STN: 4 Mar 2004
AB The aim of our study is to present expertise results of the IRMA BNP Cis bio international assay kit. Repetability for 7 standards and 3 pools (level: 9, 345, 820 pg/ml) is very acceptable (CV of pools: 9, 6 and 3%, respectively). Reproductibility is also good (3 pools tested with 3 different batches to 3 times of the shelf life of the kit): CV are lower than 10% and the performance of the kit is **stable.** Dilution and recovery tests are excellent (coefficients r(2) > 0.99; percentages of recovery > 80%). Detection limit is 1.8 pg/ml. Normal values of BNP have been established on 49 subjects devoid of any cardiac pathology (mean: 7.2 ± 5.6 pg/ml; median: 5.6 pg/ml). The clinical study (153 patients) compared plasma BNP levels and left ventricular ejection fractions. In conclusion, IRMA BNP assay kit presents all technical qualities to be used for clinical applications.

L93 ANSWER 28 OF 37 EMBASE
ACCESSION NUMBER: 96205940 EMBASE
DOCUMENT NUMBER: 1996205940
TITLE: Comparison of N-terminal pro-atrial **natriuretic peptide** and atrial **natriuretic peptide** in human plasma as **measured** with commercially available radioimmunoassay **kits.**
AUTHOR: Boomsma F.; Bhaggoe U.M.; Man in 't Veld A.J.; Schalekamp M.A.D.H.
CORPORATE SOURCE: Cardiovascular Res. Institute COEUR, Division of Internal Medicine I, Dijkzigt/Erasmus University, Dr. Molewaterplein 40,3015 GD Rotterdam, Netherlands
SOURCE: Clinica Chimica Acta, (1996) Vol. 252, No. 1, pp. 41-49. . ISSN: 0009-8981 CODEN: CCATAR
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery
020 Gerontology and Geriatrics
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 21 Aug 1996
Last Updated on STN: 21 Aug 1996
ED Entered STN: 21 Aug 1996
Last Updated on STN: 21 Aug 1996
AB Atrial natriuretic peptide (ANP) has become an important parameter for assessing the condition of patients with cardia disease. Recently, attention has also focused on N-terminal pro-atrial natriuretic peptide (NtproANP) in this context. NtproANP circulates in plasma in higher concentration, is more **stable** ex vivo, and may be a better parameter for cardiac function over time. We have evaluated a new commercially available radioimmunoassay kit for NtproANP and compared results and method withthose of ANP measurements. The NtproANP kit was found to be reliable and easy to use (no plasma extraction step is necessary), with good reproducibility (coefficients of variation 7-15%). Normal values in 15 healthy laboratory workers, 25 healthy elderly subjects and 25 patients with heart failure were 207 ± 70, 368 ± 134 and 1206 ± 860 pmol/l, respectively, 8.3, 11.8 and 13.0 times higher, respectively, than corresponding ANP concentrations. NtproANP correlated

well with ANP (r 0.64-0.78). We conclude that plasma NtproANP measurement may be a good alternative to plasma ANP measurement: technically, it is easier to perform, and NtproANP is more **stable** in plasma. Whether NtproANP is a better diagnostic and prognostic parameter than ANP remains to be further established.

L93 ANSWER 29 OF 37 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 90085909 EMBASE
DOCUMENT NUMBER: 1990085909
TITLE: **Radioreceptor assay** for atrial **natriuretic peptide** using purified receptor.
AUTHOR: Mizuno T.; Uchida K.; Shimonaka M.; Akita M.; Hirose S.; Yikumura T.; Saitoh M.; Ikemoto F.; Yamamoto K.
CORPORATE SOURCE: Department of Biological Sciences, Tokyo Institute of Technology, Ookayama, Meguroku, Tokyo 152, Japan
SOURCE: Biomedical Research, (1990) Vol. 11, No. 1, pp. 29-34. ISSN: 0388-6107 CODEN: BRESD5
COUNTRY: Japan
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 1991
Last Updated on STN: 13 Dec 1991
ED Entered STN: 13 Dec 1991
Last Updated on STN: 13 Dec 1991

AB A rapid and sensitive radioreceptor assay for atrial natriuretic peptide (ANP) has been developed using ANP receptors purified from bovine lung. The active ANP receptor was purified by a combination of Triton X-100 extraction of bovine lung membranes, ammonium sulfate fractionation, and affinity chromatography on ANP-Affi-Gel 10. The purified receptor preparation was more than 95% pure as estimated by densitometric scanning of its sodium dodecyl sulfate-polyacrylamide gel electrophoretic patterns, **stable** at least for 3 months if stored at 4°C, and resistant to repeated freezing and thawing. Kinetic analysis indicated that the binding of ANP to the receptor is fast, reaching a plateau within an hour (t(1/2) = 15 min). However, dissociation of the ANP · receptor complex was extremely slow (t(1/2) > 50 h). These **stability** and kinetic properties of the purified ANP receptor were desirable for developing receptor assays. The radioreceptor assay reported here is based on the competition between ANP in unknown samples and a fixed amount of 125I-ANP for a limited amount of receptor sites. The sensitivity was 0.3 pg/tube; cross-reactivities with the ANP analogs atriopeptin I and III were 18% and 10%, respectively; the assay usually completed within 1 h making the method practically advantageous over immunoassays that take 2-3 days. When applied to the measurements of human plasma levels of ANP, the assay yielded values that correlate well with those obtained by the existing radioimmunoassays.

L93 ANSWER 30 OF 37 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 88048701 EMBASE
DOCUMENT NUMBER: 1988048701
TITLE: A highly sensitive **radioreceptor assay** for atrial **natriuretic peptide** in rat plasma.
AUTHOR: Ballermann B.J.
CORPORATE SOURCE: Laboratory of Kidney and Electrolyte Physiology, Brigham

and Women's Hospital, Boston, MA 02115, United States
SOURCE: American Journal of Physiology - Renal Fluid and Electrolyte Physiology, (1988) Vol. 254/1 (23, No. 1), pp. F159-F163. .
ISSN: 0002-9513 CODEN: AJPFDM
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 002 Physiology
018 Cardiovascular Diseases and Cardiovascular Surgery
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 11 Dec 1991
Last Updated on STN: 11 Dec 1991
ED Entered STN: 11 Dec 1991
Last Updated on STN: 11 Dec 1991
AB To enable serial measurements of plasma atrial natriuretic peptide (ANP) concentrations in the rat, a microradioreceptor assay (RRA) for this hormone was developed. Glomerular microsomes bearing ANP receptors were used to bind ANP. The smallest quantity of ANP detectable by this method was 0.2 fmol/sample. By contrast, a radioimmunoassay for ANP was sensitive to 2.4 fmol/sample. The intra- and interassay coefficients of variation for the RRA were 4.1 and 11.6%, respectively. Recovery of 10, 20, 50 and 100 pM synthetic ANP added to unextracted rat plasma was essentially 100%. Biologically inactive, synthetic amino- and carboxy-terminal ANP fragments added to rat plasma were not detected. Plasma ANP was **stable** when measured four consecutive times at 90-min intervals in 10 fasting rats. In a separate group of rats, fasting plasma ANP levels averaged 34 ± 3 and rose to 57 ± 5 pM in the postprandial state ($P < 0.001$), whereas levels in fasting time controls remained constant. It is concluded that the RRA for ANP described here detects ANP in microliter quantities of unextracted rat plasma. Thus serial measurements of ANP concentrations can be undertaken in rats without inducing major changes in the volume status.

L93 ANSWER 31 OF 37 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-562726 [57] WPIX
CROSS REFERENCE: 2003-801121 [75]
DOC. NO. NON-CPI: N2005-461369
DOC. NO. CPI: C2005-169823
TITLE: Apparatus for enhancing dynamic range of assay of presence, absence, activity or concentration of target analytes in samples, has containers for receiving samples, assay reagents and computer system for detecting light signal.
DERWENT CLASS: B04 D16 S03 T01
INVENTOR(S): KEYS, D A; REDDY, P M
PATENT ASSIGNEE(S): (KEYS-I) KEYS D A; (REDD-I) REDDY P M
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2005170409	A1	20050804	(200557)*		19

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2005170409	A1 Div ex	US 2001-32790	20011024
		US 2005-52219	20050208

FILING DETAILS:

PATENT NO	KIND	PATENT NO
US 2005170409	A1 Div ex	US 6867005

PRIORITY APPLN. INFO: US 2001-32790 20011024; US 2005-52219 20050208

AB US2005170409 A UPAB: 20050907

NOVELTY - An apparatus for enhancing the dynamic range of an assay of the presence, absence, activity or concentration of two or more target analytes in one or more samples, by the emission of a light signal, comprises one or more containers for receiving a portion of samples, and assay reagents that generates light signal, and a computer system comprising a charge coupled device (CCD) camera detector for detecting light signal and generate data.

DETAILED DESCRIPTION - An apparatus (I) for enhancing the dynamic range of an assay of the presence, absence, activity or concentration of two or more target analytes in one or more samples, where the presence, absence, activity or concentration of the target analytes is assayed by the emission or quenching of a light signal, comprises:

(A) one or more containers for receiving a portion of the one or more samples, the containers additionally containing assay reagents comprising a compound that, in response to the presence of a target analyte causes a detectable light signal; and

(B) a computer system (CS) comprising a charge coupled device (CCD) camera detector, the computer system being specially adapted to detect the light signal and generate data corresponding to the detected signal, the computer system additionally processing a capability for comparing the generated data with data corresponding to the light signal generated by a known concentration of the target analyte in a known dynamic range of the assay and report the presence, absence, activity or concentration of the target analyte, where the computer system causes the CCD camera detector to independently detect sufficient light signal for each of the target analytes to ensure that the reported presence, absence, activity or concentration of each target analyte is determined using data corresponding to a light signal that is within the known dynamic range of the assay for that target analyte, and where, for a target analytes, the computer system causes the CCD camera detector to detect light signal:

(i) cumulatively until a total detected light signal is obtained that is within the known dynamic range of the assay for the target analyte, and where the total detected light signal is used to determine the presence, absence, activity or concentration of the target analyte; or

(ii) discontinuously at more than one time interval such that a detected light signal is obtained that is within the known dynamic range of the assay for the target analyte, and where the total detected light signal within the known dynamic range of the assay for the target analyte is used to determine the presence, absence, activity or concentration of the target analyte.

An INDEPENDENT CLAIM is also included for enhancing the dynamic range of an assay of the presence, absence, activity or concentration of two or more target analytes in one or more samples, where the presence, absence, activity or concentration of the target analytes is assayed by the emission or quenching of a light signal, involves:

(A) conducting an assay for the presence, absence, activity or

concentration of each of the target analytes in the one or more samples, where the assays each cause light signals to be emitted or quenched;

(B) causing CS to compare the generated data using data corresponding to the light signal generated by a known concentration of the target analyte in a known dynamic range of the assay and report the presence, absence, activity or concentration of the target analyte.

USE - (I) is useful for enhancing the dynamic range of an assay of the presence, absence, activity or concentration of two or more target analytes in one or more samples (claimed).

ADVANTAGE - (I) simultaneously and sequentially assays the presence, absence, activity or concentration of the more than one target analyte in the same sample (claimed).

Dwg.0/3

L93 ANSWER 32 OF 37 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-444149 [45] WPIX
DOC. NO. NON-CPI: N2005-360933
DOC. NO. CPI: C2005-135988
TITLE: **Stable liquid** reference solution for assays for detecting presence or amount of cardiac marker(s) in sample, has reference polypeptide, control, and **stabilizing** solution with amino acid(s) having basic side chain and **stabilizing** protein.
DERWENT CLASS: B04 S03
INVENTOR(S): CHAN, S; TODTLEBEN, J; CHAN, S P; TODTLEBEN, J C
PATENT ASSIGNEE(S): (BECI) BECKMAN COULTER INC
COUNTRY COUNT: 108
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2005136542	A1	20050623	(200545)*		6
WO 2005066604	A1	20050721	(200548)	EN	
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LT LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
EP 1695060	A1	20060830	(200657)	EN	
R: DE FR GB					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2005136542	A1	US 2003-741403	20031219
WO 2005066604	A1	WO 2004-US40129	20041201
EP 1695060	A1	EP 2004-812603	20041201
		WO 2004-US40129	20041201

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1695060	A1 Based on	WO 2005066604

PRIORITY APPLN. INFO: US 2003-741403 20031219

AB US2005136542 A UPAB: 20050715

NOVELTY - A **stable liquid** reference solution for assays for detecting presence or amount of a cardiac marker(s) present in a sample, comprises a reference polypeptide; a control comprising a measurable quantity of a reference polypeptide for each cardiac marker being detected; and a **stabilizing** solution comprising amino acid(s) having a basic side chain and a **stabilizing** protein.

DETAILED DESCRIPTION - A **stable liquid** reference solution for assays for detecting presence or amount of a cardiac marker(s) present in a sample, comprises a reference polypeptide; a control comprising a measurable quantity of a reference polypeptide for each cardiac marker being detected; and a **stabilizing** solution comprising amino acid(s) having a basic side chain and a **stabilizing** protein. The reference polypeptide comprises a native troponin I; native troponin I-C complex; native troponin I-T-C complex; synthetic and recombinant troponin I-T-C complex; or native, synthetic and recombinant B-type natriuretic peptide. The cardiac marker(s) comprises troponin I or B-type natriuretic peptide.

INDEPENDENT CLAIMS are also included for:

(1) a **stable liquid** control for assays for detecting the presence or amount of different polypeptide analytes present in a sample, where at least one polypeptide **analyte** comprises troponin I or B-type **natriuretic peptide** (BNP), the control comprising reference polypeptides, so that one reference polypeptide is included for each polypeptide analyte being detected; and a **stabilizing** solution comprising amino acid(s) comprising arginine, lysine, or histidine, and a **stabilizing** protein;

(2) a **stable liquid** reference solution for immunoassays for detecting the presence or amount of a B-type **natriuretic peptide** in a sample comprising a **measurable** amount of the B-type **natriuretic peptide**, and a **stabilizing** solution as above with a **stabilizing** protein comprising bovine serum albumin or human albumin, a chelating agent and a buffered media;

(3) a method for increasing storage stability of a **liquid** reference solution for assays for detecting the presence or amount of a cardiac marker in a sample, comprising incorporating into a buffered media a reference polypeptide for the cardiac marker being detected comprising native troponin or B-type natriuretic peptide; adding amino acid(s) as above to the buffered media, and adding a **stabilizing** protein;

(4) a method of assuring the quality of an immunoassay test to detect the presence or amount of a cardiac marker, comprising using a reference solution that comprises a reference polypeptide comprising native troponin or B-type natriuretic peptide, and a **stabilizing** solution as above with the **stabilizing** protein as an unknown sample with the immunoassay test; and

(5) an immunoassay kit comprising a first antibody that binds to one epitopic site of a cardiac marker as above and a second antibody that binds to a different epitopic site of the cardiac marker, where at least one of the antibodies is labeled and further comprising a set of **stable liquid** calibrators, with each calibrator comprising a known quantity of a reference comprising native troponin I, native troponin I-C complex, native troponin I-T-C complex, synthetic and recombinant troponin I-T-C complex, native, or synthetic and recombinant B-type natriuretic peptide, and a **stabilizing** solution as above.

USE - For assays for detecting presence or amount of a cardiac marker(s) present in a sample (claimed) useful in testing and confirming the accuracy and reliability of a diagnostic assay test and/or an instrument system.

ADVANTAGE - The inventive **stable liquid** reference solution remains **stable** in refrigerated temperatures (2-10 deg. C) over a period of days so that clinical sites can readily perform assays and quickly diagnose and assess coronary health and other disease states. It is also **stable** in the **liquid** form for at least 7 days at room temperature or at 37 deg. C and as long as about 9 weeks at 4 deg. C.
Dwg.0/0

ABEX UPTX: 20050715
EXAMPLE - A stable liquid reference solution containing native troponin I (purified from human heart tissue) in the stabilizing solution was prepared. The troponin polypeptides was incorporated into a stabilizing solution that included a buffer solution with 1% (w/v) bovine serum albumin, 5% arginine (w/v) and a non-ionic surfactant; and polysorbate 80 at 0.15% (v/v). The pH of the solution with troponin I was adjusted to 6.8+/-0.1. The solution also included preservatives commonly found in reference solutions. Native troponin I antigen HTI ITC were incorporated into the liquid reference solutions. The solutions were tested using an ACCESS Immunoassay System with the ACCESS AccuTnI commercially available test kit at 3, 5, and 11 days following storage of the reference solutions at 45 degrees C The results showed a 104.1% recovery at 3 days, a 94.7% recovery at day 5, and a 96.5% recovery at 11 days.

L93 ANSWER 33 OF 37 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-660294 [68] WPIX
DOC. NO. NON-CPI: N2005-540897
DOC. NO. CPI: C2005-199841
TITLE: Diagnosing risk of patient suffering from cardiovascular complication as result of intravasal volume increase, by measuring cardiac hormone level, comparing measured level to known level associated with various grades of risk in patient.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): HESS, G; HORSCH, A
PATENT ASSIGNEE(S): (HOFF) HOFFMANN LA ROCHE & CO AG F; (HOFF) ROCHE DIAGNOSTICS GMBH; (HESS-I) HESS G; (HORS-I) HORSCH A
COUNTRY COUNT: 39
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1577673	A1	20050921	(200568)*		51
R: AL AT BA BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK NL PL PT RO SE SI SK TR YU					
CA 2500886	A1	20050915	(200568)	EN	
JP 2005274569	A	20051006	(200568)		38
US 2005239138	A1	20051027	(200571)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1577673	A1	EP 2005-5356	20050311
CA 2500886	A1	CA 2005-2500886	20050314
JP 2005274569	A	JP 2005-72768	20050315
US 2005239138	A1	US 2005-79162	20050314

PRIORITY APPLN. INFO: EP 2004-6080 20040315
AB EP 1577673 A UPAB: 20051024

NOVELTY - Diagnosing (M1) the risk of a patient suffering from a cardiovascular complication as a consequence of the increase of intravasal volume, involves measuring the level of a cardiac hormone, preferably in vitro, and diagnosing the risk of the patient by comparing the measured level to one or more known level(s) associated with different grades of risk in a patient.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) use of diagnostic means capable of **measuring** a patient's level of a cardiac hormone, preferably **natriuretic peptide**, in vitro, for diagnosing the patient's risk of suffering from a cardiovascular complication as a consequence of an increase of intravasal volume; and

(2) deciding (M2) about the administration to a patient an infusion, transfusion or a drug causing volume overload, involves measuring the level of a cardiac hormone in the patient, preferably in vitro, comparing the measured level with one or more known level(s) associated with different grades of risk in a patient, optionally initiating an examination of the patient by a cardiologist, and recommending or refraining the administration by infusion, transfusion or drug, optionally in consideration of the result of the patient's examination by the cardiologist.

USE - (M1) is useful for diagnosing the risk of a patient suffering from a cardiovascular complication as a consequence of the increase of intravasal volume, where the cardiovascular complication is coronary heart disease, acute coronary syndrome, myocardial infarction, left ventricular dysfunction or congestive heart failure. (M2) is useful for deciding about the administration to a patient an infusion, transfusion or a drug causing volume overload, where the drug is a selective Cox-2 inhibitor (claimed).

ADVANTAGE - (M1) easily, cost effectively and reliably diagnosis the risk of a patient suffering from a cardiovascular complication as a consequence of the increase of intravasal volume, where the diagnosis can be performed by cardiologists and non-cardiologists.

DESCRIPTION OF DRAWING(S) - The figure is a graph representing the N-terminal-pro brain natriuretic peptide levels in males according to left ventricular ejection fraction.

Dwg.15/28

ABEX UPTX: 20051024

EXAMPLE - Patients (473) suspected of having cardiac disorders were taken for the study, in which 78 individuals had a history of myocardial infarction. The patient's medical history, physical examination and echocardiogram, and the left ventricular ejection fraction (LVEF) were recorded. The blood (10 ml) was drawn, and centrifuged. The NT-proBNP in blood was analyzed using electrochemoluminescence immunoassay. The biotin labeled IgG capture antibody, ruthenium-labeled F (ab')2 signal antibody and 20 mul of sample were incubated at 37degreesC for 9 minutes. The streptavidin-coated magnetic microparticles were added and the mixture was incubated for additional 9 minutes. The obtained mixture was transferred to the measuring cell of the system. The unbound label was removed by washing the cell with buffer. The voltage was applied to electrode in presence of tri-propyl amine containing buffer and the resulting signal was recorded by a photomultiplier. Thus the NT-proBNP levels in patients was measured. The results indicated that the individuals with myocardial infarction had higher NT-proBNP levels than those without myocardial infarction.

L93 ANSWER 34 OF 37 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2005-013096 [01] WPIX
DOC. NO. NON-CPI: N2005-010595
DOC. NO. CPI: C2005-003585
TITLE: Diagnosis and risk stratification of patient possibly

with clinical condition, e.g. acute coronary syndrome, comprises obtaining sample(s) of substance stream that has been in contact with tissue suspected of undergoing clinical condition.

DERWENT CLASS: B04 P31 S03 S05 T01

INVENTOR(S): CROSBY, P; MORRIS, D; SOANE, M; CROSBY, P A; MORRIS, D L; SOANE, M M

PATENT ASSIGNEE(S): (ISCH-N) ISCHEMIA TECHNOLOGIES INC

COUNTRY COUNT: 109

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2004103150	A2	20041202	(200501)*	EN	50
RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
US 2005004485	A1	20050106	(200504)		
EP 1633244	A2	20060315	(200620)	EN	
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IT LI LT LU LV MC MK NL PL PT RO SE SI SK TR					
AU 2004240557	A1	20041202	(200628)		
US 2006135875	A1	20060622	(200642)		
US 7074194	B2	20060711	(200646)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004103150	A2	WO 2004-US14412	20040505
US 2005004485	A1	US 2003-441155	20030519
EP 1633244	A2	EP 2004-751679	20040505
		WO 2004-US14412	20040505
AU 2004240557	A1	AU 2004-240557	20040505
US 2006135875	A1 Cont of	US 2003-441155	20030519
		US 2005-317831	20051222
US 7074194	B2	US 2003-441155	20030519

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1633244	A2 Based on	WO 2004103150
AU 2004240557	A1 Based on	WO 2004103150

PRIORITY APPLN. INFO: US 2003-441155 20030519; US 2005-317831 20051222

AB WO2004103150 A UPAB: 20050103

NOVELTY - Diagnosis and risk stratification of patient (16) possibly with a clinical condition comprises obtaining from the patient a sample(s) of substance stream that has been in contact with a tissue suspected of undergoing the clinical condition.

DETAILED DESCRIPTION - Diagnosis and risk stratification of patient possibly with the clinical condition comprises:

(a) obtaining from the patient a sample(s) of substance stream that has been in contact with a tissue suspected of undergoing the clinical

condition;

(b) conducting first in vitro diagnosis assay on the sample and optionally additional in vitro diagnosis assays;

(c) measuring and analyzing the patient's electrocardiogram (ECG); and

(d) applying an algorithm to combine the results of the assay(s) and electrocardiogram using an algorithm to provide a positive or negative diagnosis or risk stratification of the clinical condition.

An INDEPENDENT CLAIM is also included for an apparatus for diagnosis of clinical condition or estimating the probability of the presence of the condition in a patient comprising:

(a) electronic module housing (10) having display mechanism (12);

(b) data entry and control mechanism;

(c) mechanism for measuring an ECG;

(d) aperture (19) containing a reader mechanism;

(e) analysis mechanism in electrical continuity with the data entry and control mechanism, ECG mechanism, and reader mechanism; power source; and

(f) optionally a link to a laboratory or hospital information system.

The analysis mechanism can analyze signals each mechanism. The aperture is adapted to receive a sample analysis strip for conducting an in vitro diagnostic assay on a patient sample of a substance stream. The reader is adapted to read results of the assay. The analyzer receives signals from the ECG mechanism and data entry and control mechanism, and upon insertion of the strip into the aperture from the reader mechanism, the analyzer mechanism transmits analyzed results to the display mechanism.

USE - For the diagnosis and risk stratification of patient possibly with a clinical condition, e.g. acute coronary syndrome, acute myocardial infarction, **stable** angina, or unstable angina (claimed).

ADVANTAGE - The invention provides more and better tools for emergency medicine physicians and others. It makes reliable assessment of a patient's risk of cardiac ischemia at presentation using existing sources of diagnostic information and combinations of new and existing sources of information.

DESCRIPTION OF DRAWING(S) - The figure is a diagrammatic illustration of a device that includes apparatus for ECG analysis in conjunction with apparatus for performing in vitro diagnostic test(s).

Electronic module housing 10

ECG results 11

Display mechanism 12

Patient 16

Aperture 19

Dwg.2/10

L93 ANSWER 35 OF 37 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 1992-133113 [17] WPIX

CROSS REFERENCE: 1992-133111 [17]; 1992-133112 [17]; 1992-167095 [20]

DOC. NO. CPI: C1992-062303

TITLE: New cyclo peptide(s) are atrial natriuretic factor agonists - useful as hypotensives, vasodilators, spasmolytics and broncholytics, and as **ligands** in receptor **binding** assays.

DERWENT CLASS: B04

INVENTOR(S): HEINRICHS, S; PALLUK, R; SCHNORRENBERG, G; SCHNORRENB, G

PATENT ASSIGNEE(S): (BOEH) BOEHRINGER INGELHEIM INT GMBH; (BOEH) BOEHRINGER INGELHEIM KG; (BOEH) BOEHRINGER INGELHEIM

COUNTRY COUNT: 18

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 4032271	A	19920416	(199217)*		18
FI 9301499	A	19930402	(199326)		
NO 9301341	A	19930407	(199329)		
EP 552238	A1	19930728	(199330)	GE	144
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE					
HU 63859	T	19931028	(199348)		
CS 9300618	A2	19940119	(199410)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 4032271	A	DE 1990-4032271	19901011
FI 9301499	A	WO 1991-EP1934	19911010
		FI 1993-1499	19930402
NO 9301341	A	WO 1991-EP1934	19911010
		NO 1993-1341	19930407
EP 552238	A1	EP 1991-918322	19911010
		WO 1991-EP1934	19911010
HU 63859	T	WO 1991-EP1934	19911010
		HU 1993-1054	19911010
CS 9300618	A2	CS 1993-618	19911010

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 552238	A1 Based on	WO 9206998
HU 63859	T Based on	WO 9206998

PRIORITY APPLN. INFO: DE 1990-4032268 19901011; DE 1990-4032269 19901011; DE 1990-4032271 19901011; DE 1991-4117733 19910530; WO 1991-EP1934 19911010

AB DE 4032271 A UPAB: 19931116
Cyclic peptides of formula (I) and their pharmaceutically acceptable salts are new; A = NH-(CH2)-nCHR-CO; n = 1-11; R = NHX, OX, SX or NHY; X = H; benzoyl, cyclohexyloxycarbonyl or benzyloxycarbonyl (all opt. substd.); 2-, 3- or 4-pyridylmethoxycarbonyl, or tosyl; Y = 1-4C alkyl (opt. substd. by aryl); B = bond, Phe or alpha-aminoacid residue with 1 or 2 side chains, at least one of these containing 1-4 N-containing gps.; C = alpha-aminoacid residue with 1 or 2 opt. O-containing alkyl side chains, each of which can be substd. by 1 or 2 of 4-7C cycloalkyl, phenyl (opt. substd. by e.g. NO2); naphthyl or a 5-6 membered aromatic heterocycle with 2N; one N plus one O or S; or N, S or O; pref. thienyl, furyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl; pyridazinyl, indolyl, (iso)quinolyl, chromanyl, thiazolyl, oxazolyl or morpholino.
D and E = Gly or alpha-aminoacid residue in which the side chain has no functional gps., or together they complete -NH-(CH2)-mCO (m = 2-11) or a peptide template; F and I are as B but not bond or Phe; G and K are alpha-aminoacid residue, with 1 or 2 lipophilic side chains; H = bond or alpha-aminoacid residue in which the side chain has no functional gps. or has COOH or CONH2 as functional gps..
0/0
Dwg.0/0

L93 ANSWER 36 OF 37 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 1992-133112 [17] WPIX
CROSS REFERENCE: 1992-133111 [17]; 1992-133113 [17]; 1992-167095 [20]
DOC. NO. CPI: C1992-062302
TITLE: New cyclo peptide(s) are atrial natriuretic factor agonists - useful as hypotensives, vasodilators, spasmolytics and broncholytics, as **ligands** in receptor **binding** assays and for purificn. of antibodies.
DERWENT CLASS: B04
INVENTOR(S): HEINRICHS, S; PALLUK, R; SCHNORRENBERG, G; SCHNORRENB, G
PATENT ASSIGNEE(S): (BOEH) BOEHRINGER INGELHEIM INT GMBH; (BOEH) BOEHRINGER INGELHEIM KG; (BOEH) BOEHRINGER INGELHEIM
COUNTRY COUNT: 19
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 4032269	A	19920416	(199217)*		26
FI 9301499	A	19930402	(199326)		
NO 9301341	A	19930407	(199329)		
EP 552238	A1	19930728	(199330)	GE	144
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE					
HU 63859	T	19931028	(199348)		
CS 9300618	A2	19940119	(199410)		
JP 06501950	W	19940303	(199414)		24

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 4032269	A	DE 1990-4032269	19901011
FI 9301499	A	WO 1991-EP1934	19911010
		FI 1993-1499	19930402
NO 9301341	A	WO 1991-EP1934	19911010
		NO 1993-1341	19930407
EP 552238	A1	EP 1991-918322	19911010
		WO 1991-EP1934	19911010
HU 63859	T	WO 1991-EP1934	19911010
		HU 1993-1054	19911010
CS 9300618	A2	CS 1993-618	19911010
JP 06501950	W	JP 1991-516845	19911010
		WO 1991-EP1934	19911010

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 552238	A1 Based on	WO 9206998
HU 63859	T Based on	WO 9206998
JP 06501950	W Based on	WO 9206998

PRIORITY APPLN. INFO: DE 1990-4032268 19901011; DE 1990-4032269 19901011; DE 1990-4032271 19901011; DE 1991-4117733 19910530; WO 1991-EP1934 19911010

AB DE 4032269 A UPAB: 19931116
Cyclic peptides of formula (I) and their pharmaceutically acceptable salts are new; A = bond or a gp. NH-(CH2)-NCO; N = 1-11; B = bond or an alpha-aminoacid residue with 1 or 2 opt. O-containing alkyl side chains, each

of which can be substd. by 1 or 2 of 4-7C cycloalkyl-phenyl (opt substd. by e.g. NO2); naphthyl or a 5-6 membered aromatic heterocycle with 2N; are N plus one O or S; or one N, S or O; pref. thienyl, furyl, pyrrolyl, imidazolyl, pyrazolyl, pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, indolyl, (iso)quinolyl, chromanyl, thiazolyl, oxazolyl or morpholino; or A+B are together a peptide template; C = bond, Gly or alpha-aminoacid residue with 1 or 2 side chains at least one of which contains 1-4 N-containing gps., D is as B but not a bond; E and F are each Gly or alpha-aminoacid residue in which the side chain contains no functional gps., or together they are NH-CH2)-MCO (M=2-11) or a peptide template; G is as C but not a bond; H = alpha amino acid residue which has 1 or 2 lipophilic side chains; I = bond or alpha amino acid residue in which the side chains contain (a) no functional gps. or (b) COOH or CONH2 as functional gps.; K is as G. L is as H.
0/0
Dwg.0/0

L93 ANSWER 37 OF 37 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 1992-133111 [17] WPIX
CROSS REFERENCE: 1992-133112 [17]; 1992-133113 [17]; 1992-167095 [20]
DOC. NO. CPI: C1992-062301
TITLE: New cyclo-peptide(s) are atrial natriuretic factor agonists - useful as hypotensives, vasodilators, spasmolytics and broncholytics, as **ligands** in receptor **binding** tests and for antibody purification.
DERWENT CLASS: B04
INVENTOR(S): HEINRICHS, S; PALLUK, R; SCHNORRENBERG, G; SCHNORRENB, G
PATENT ASSIGNEE(S): (BOEH) BOEHRINGER INGELHEIM INT GMBH; (BOEH) BOEHRINGER INGELHEIM KG; (BOEH) BOEHRINGER INGELHEIM
COUNTRY COUNT: 19
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
DE 4032268	A	19920416	(199217)*		20
FI 9301499	A	19930402	(199326)		
NO 9301341	A	19930407	(199329)		
EP 552238	A1	19930728	(199330)	GE	144
R: AT BE CH DE DK ES FR GB GR IT LI LU NL SE					
HU 63859	T	19931028	(199348)		
CS 9300618	A2	19940119	(199410)		
JP 06501950	W	19940303	(199414)		24

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
DE 4032268	A	DE 1990-4032268	19901011
FI 9301499	A	WO 1991-EP1934	19911010
		FI 1993-1499	19930402
NO 9301341	A	WO 1991-EP1934	19911010
		NO 1993-1341	19930407
EP 552238	A1	EP 1991-918322	19911010
		WO 1991-EP1934	19911010
HU 63859	T	WO 1991-EP1934	19911010
		HU 1993-1054	19911010
CS 9300618	A2	CS 1993-618	19911010
JP 06501950	W	JP 1991-516845	19911010
		WO 1991-EP1934	19911010

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 552238	A1 Based on	WO 9206998
HU 63859	T Based on	WO 9206998
JP 06501950	W Based on	WO 9206998

PRIORITY APPLN. INFO: DE 1990-4032268 19901011; DE
1990-4032269 19901011; DE
1990-4032271 19901011; DE
1991-4117733 19910530; WO
1991-EP1934 19911010

AB DE 4032268 A UPAB: 19931116

Cyclic peptides and their pharmaceutically acceptable salts are of formula (I) where AS = bond or a gp. NH(CH2)nCo; n = 1-11; B = bond or an alpha-aminoacid residue with 1 or 2 opt. O-containing alkyl sides chains, each of which can be substd. by 1 or 2 of 4-7C cycloalkyl; phenyl (opt. substd. e.g. NO2); naphthyl or a 5-6 membered aromatic heterocycle pref. thienyl, furyl, pyrrolyl etc. C = bond or alpha-aminoacid residue with 1 or 2 side chains, at least one containing 1-4 N-containing gps.; D is as B but not a bond; E and F are each Gly or alpha-aminoacid residue in which the side chain contains no functional gps., or together they are NH(CH2)m-CO (m=2-11) or a peptide template; G is as C but not a bond; H = alpha-aminoacid residue which has 1 or 2 lipophilic side chains; I = bond or alpha-aminoacid reisude in which the side chains contain (a) no functional gps. or (b) COOH or CONH2 as functional gp.; K is as G; L is as H; M is as E(considered alone).

USE/ADVANTAGE - (I) are agonists of atrial natriuretic peptide (ANO) will specific affinity for ANP receptors. They are useful as antihypertensive/hypotensive, diuretic/saliuretic; vasadilating, spasmolytic and broncholytic agents. Since (I) are smaller molecules than ANP, they are easier and cheaper to prepare; have higher bioavailability, (especially when given transdermally) and, greater metabolic stability.

0/0

Dwg.0/0

```
=> d his full

     (FILE 'HOME' ENTERED AT 10:18:51 ON 14 SEP 2006)
               D SAVED

     FILE 'CAPLUS' ENTERED AT 10:19:13 ON 14 SEP 2006
               ACTIVATE GIT031AU/A
               ---------
L1   (       965)SEA ABB=ON  PLU=ON  PARSONS R?/AU
L2   (         7)SEA ABB=ON  PLU=ON  DAGHFAL D?/AU
L3   (         1)SEA ABB=ON  PLU=ON  LIPOWSKY C?/AU
L4   (        73)SEA ABB=ON  PLU=ON  WEIGAND R?/AU
L5   (       136)SEA ABB=ON  PLU=ON  FRIESE J?/AU
L6   (     10806)SEA ABB=ON  PLU=ON  NATRIURETIC PEPTIDE
L7             2 SEA ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5) AND L6
               ---------
               ACTIVATE GIT031CA/A
               ---------
L8   (        11)SEA ABB=ON  PLU=ON  STABILIZING AGENTS+PFT,NT/CT (L) NATRIURETI
               C
L9   (         5)SEA ABB=ON  PLU=ON  STABILITY/CT (L) NATRIURETIC
L10           12 SEA ABB=ON  PLU=ON  L8 OR L9
               ---------

     FILE 'BIOSIS' ENTERED AT 10:20:35 ON 14 SEP 2006
L11            6 SEA ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5) AND L6
               D SCAN
L12        16678 SEA ABB=ON  PLU=ON  NATRIURET? (1A) PEPTIDE
L13       423241 SEA ABB=ON  PLU=ON  (STABLE OR STABILI?)
L14          491 SEA ABB=ON  PLU=ON  L12 AND L13
L15          142 SEA ABB=ON  PLU=ON  L12 (S) L13
L16          124 SEA ABB=ON  PLU=ON  L12 (15A) L13
L17      4456463 SEA ABB=ON  PLU=ON  MEASUR? OR TEST? OR ASSAY? OR ANALY?
L18           79 SEA ABB=ON  PLU=ON  L16 AND L17
L19           63 SEA ABB=ON  PLU=ON  L18 NOT STABLE ANGINA
               D SCAN
L20           20 SEA ABB=ON  PLU=ON  L19 AND (STABILITY OR PROBNP OR CLINICAL
               OR AXSYM OR SUCROSE OR STABILIZATION)/TI
               D SCAN
L21           19 SEA ABB=ON  PLU=ON  L20 NOT STABLE CORONARY/TI

     FILE 'MEDLINE' ENTERED AT 10:36:40 ON 14 SEP 2006
L22        14925 SEA ABB=ON  PLU=ON  NATRIURETIC PEPTIDES+NT/CT
L23            0 SEA ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5) AND L6
L24       417776 SEA ABB=ON  PLU=ON  STABILI? OR STABL?
L25          575 SEA ABB=ON  PLU=ON  L22 AND L24
               D TRIAL 1-10
L26        12513 SEA ABB=ON  PLU=ON  NATRIURETIC (1A) PEPTIDE
L27          122 SEA ABB=ON  PLU=ON  L26 (15A) L24
L28            3 SEA ABB=ON  PLU=ON  L27 AND L22 (L) AN/CT
               D TRIAL 1-3
L29          108 SEA ABB=ON  PLU=ON  L26 (15A) L24 AND L22
               D TRIAL 1-10
L30           85 SEA ABB=ON  PLU=ON  L29 NOT (STABLE)/TI (3A) (HEART OR
               CORONARY OR ANGINA)/TI
               D TRIAL 1-10
               D TRIAL 11-21
               D TRIAL 31-45
               D TRIAL 46-60
```

```
                D TRIAL 61-75
                D TRIAL 76-85
L31          11 SEA ABB=ON  PLU=ON  L30 AND (WHOLE BLOOD OR ADRENERGIC OR
                STORAGE OR YEARS OR STABILIZATION)/TI
                D TRIAL 1-11

     FILE 'EMBASE' ENTERED AT 11:00:07 ON 14 SEP 2006
L32           0 SEA ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5) AND L6
                D QUE L7
                E NATRIURETIC PEPTIDE+ALL/CT
L33       12000 SEA ABB=ON  PLU=ON  NATRIURETIC (1A) PEPTIDE
L34      377785 SEA ABB=ON  PLU=ON  STABLE OR STABILI?
L35         108 SEA ABB=ON  PLU=ON  L33 (15A) L34
                D TRIAL 1-10
L*** DEL     79 S L35 NOT (STABLE (3A) HEART OR CORONARY OR ISCHEMI?)/TI
                D TRIAL 1-10
L36          62 SEA ABB=ON  PLU=ON  L35 NOT (STABLE (3A) HEART OR CORONARY OR
                ISCHEMI? OR ANGINA OR PULMONARY OR EMBOLISM)
                D TRIAL 1-15
                D TRIAL 16-32
                D TRIAL 33-48
                D TRIAL 49-62
L37          23 SEA ABB=ON  PLU=ON  L36 AND (ELECSYS OR STABIILZ? OR THAW OR
                LEFT OR PROLONGED OR RAPID OR ATRIAL NATRIURETIC)/TI
L38          12 SEA ABB=ON  PLU=ON  L37 AND (SCAN? OR MEASUR? OR DIAGNOS? OR
                ASSAY? OR TEST?)
                D TRIAL 1-12
L39          11 SEA ABB=ON  PLU=ON  L37 NOT L38
                D TRIAL 1-11

     FILE 'WPIX' ENTERED AT 12:13:04 ON 14 SEP 2006
L40           3 SEA ABB=ON  PLU=ON  (L1 OR L2 OR L3 OR L4 OR L5) AND L6
                D SCAN
                D TRIAL L40 1-3

     FILE 'CAPLUS' ENTERED AT 12:14:36 ON 14 SEP 2006
                D QUE L10
L41       10883 SEA ABB=ON  PLU=ON  NATRIURETIC (1A) PEPTIDE
L42     5686097 SEA ABB=ON  PLU=ON  (CALIBRAT? OR MEASUR? OR ASSAY? OR TEST?
                OR IDENTIF?)
L43        4380 SEA ABB=ON  PLU=ON  L41 AND L42
L44        1233 SEA ABB=ON  PLU=ON  L41 (10A) L42
L45     1040820 SEA ABB=ON  PLU=ON  STABLE? OR STABILIZ?
L46          64 SEA ABB=ON  PLU=ON  L44 AND L45
L47          49 SEA ABB=ON  PLU=ON  L46 NOT STABLE (3A) (HEART OR ANGINA OR
                EMBOLI?)
                D SCAN
L48       44004 SEA ABB=ON  PLU=ON  LIQUID (3A) L42
L*** DEL   4380 S L41 AND L42
L*** DEL     64 S L49 AND L46
L*** DEL     49 S L50 NOT STABLE (3A) (HEART OR ANGINA OR EMBOLI?)
L*** DEL      0 S L51 NOT L47
L49           7 SEA ABB=ON  PLU=ON  L41 AND L48
                D SCAN
                D SCAN TI
L50           3 SEA ABB=ON  PLU=ON  L49 AND (ISOLATION OR ASSAY OR CALIBRAT?)/T
                I
                D SCAN TI L10
L51           4 SEA ABB=ON  PLU=ON  L10 AND (MEASURE? OR METHOD? OR CALIBRATOR)
                /TI NOT TRANSDERMAL/TI
```

```
     FILE 'BIOSIS' ENTERED AT 12:28:09 ON 14 SEP 2006
                D QUE L21
L52          4730 SEA ABB=ON  PLU=ON  L12 AND L42
L53          1373 SEA ABB=ON  PLU=ON  L12 (10A) L42
L54        247734 SEA ABB=ON  PLU=ON  LIQUID?
L55            36 SEA ABB=ON  PLU=ON  L53 AND L54
                D SCAN L21
L56            11 SEA ABB=ON  PLU=ON  L21 NOT (EXERCISE OR CARDIAC OR BNP)/TI
                D SCAN
L*** DEL        8 S L21 NOT L56
                D QUE L21
L57             8 SEA ABB=ON  PLU=ON  L21 NOT L56
                D SCAN
L58            35 SEA ABB=ON  PLU=ON  L55 NOT L21
                D SCAN
                D QUE L21
L59             1 SEA ABB=ON  PLU=ON  L58 AND L13
                D SCAN
L60         27012 SEA ABB=ON  PLU=ON  LIGAND (1A) BIND?
L61             1 SEA ABB=ON  PLU=ON  L58 AND L60
                D SCAN

     FILE 'MEDLINE' ENTERED AT 12:40:46 ON 14 SEP 2006
                D TRIAL L31 1-11
                D QUE L31
L62         10653 SEA ABB=ON  PLU=ON  L22/MAJ
L63       3846372 SEA ABB=ON  PLU=ON  (CALIBRAT? OR MEASUR? OR ASSAY? OR TEST?
                OR IDENTIF?)
L64          4363 SEA ABB=ON  PLU=ON  L62 AND L63
                D TRIAL 1-10
L65         23634 SEA ABB=ON  PLU=ON  LIGAND (1A) BIND?
L66         11681 SEA ABB=ON  PLU=ON  LIQUID (3A) L42
L67             8 SEA ABB=ON  PLU=ON  L62 AND L66
L68            32 SEA ABB=ON  PLU=ON  L62 AND L60
                D TRIAL L67
                D TRIAL L67 2-8
L69             1 SEA ABB=ON  PLU=ON  L67 AND UNEXTRACTED/TI
                D TRIAL L68 1-16
                D TRIAL L68 17-32

     FILE 'EMBASE' ENTERED AT 12:48:52 ON 14 SEP 2006
                D TRIAL L38 1-12
L70             5 SEA ABB=ON  PLU=ON  L38 AND (ELECSYS OR RAPID ASSAY OR
                ASSESSMENT)/TI
                D TRIAL 1-5
                D QUE L38
L71          1514 SEA ABB=ON  PLU=ON  L33 (10A) (SCAN? OR MEASUR? OR DIAGNOS? OR
                ASSAY? OR TEST?)
L72            80 SEA ABB=ON  PLU=ON  L71 AND L34
                D TRIAL 1-10
L73           349 SEA ABB=ON  PLU=ON  (NATRIURETIC/TI (1A) PEPTIDE/TI) (10A)
                (SCAN? OR MEASUR? OR DIAGNOS? OR ASSAY? OR TEST?)/TI
                D QUE L34
L74            22 SEA ABB=ON  PLU=ON  L73 AND L34
                D TRIAL 1-22
L75             4 SEA ABB=ON  PLU=ON  L74 AND (KIT OR KITS OR RADIORECEPTOR)/TI

     FILE 'WPIX' ENTERED AT 12:59:42 ON 14 SEP 2006
L76           472 SEA ABB=ON  PLU=ON  NATRIURET? (1A) PEPTIDE
```

```
L77     1575921 SEA ABB=ON  PLU=ON  MEASUR? OR TEST? OR ASSAY? OR ANALY? OR
                IDENTIF?
L78          48 SEA ABB=ON  PLU=ON  L76 (10A) L77
                D TRIAL L40 1-3
L79     1135746 SEA ABB=ON  PLU=ON  LIQUID OR PH
L80           5 SEA ABB=ON  PLU=ON  L78 AND L79
L81           2 SEA ABB=ON  PLU=ON  L80 NOT L40
                D TRIAL 1-2
L82           1 SEA ABB=ON  PLU=ON  L81 AND LIQUID/TI
L83        6177 SEA ABB=ON  PLU=ON  LIGAND (3A) BIND?
L84           8 SEA ABB=ON  PLU=ON  L78 AND L83
L85           5 SEA ABB=ON  PLU=ON  L84 NOT L40
                D TRIAL 1-5
L86      394854 SEA ABB=ON  PLU=ON  STABLE? OR STABILIZ?
L87           6 SEA ABB=ON  PLU=ON  L78 AND L86
                D SCAN

     FILE 'CAPLUS' ENTERED AT 13:15:57 ON 14 SEP 2006
                D QUE L7

     FILE 'BIOSIS' ENTERED AT 13:16:10 ON 14 SEP 2006
                D QUE L11

     FILE 'MEDLINE' ENTERED AT 13:16:17 ON 14 SEP 2006
                D QUE L23

     FILE 'EMBASE' ENTERED AT 13:16:26 ON 14 SEP 2006
                D QUE L32

     FILE 'WPIX' ENTERED AT 13:16:33 ON 14 SEP 2006
                D QUE L40

     FILE 'CAPLUS, BIOSIS, WPIX' ENTERED AT 13:16:46 ON 14 SEP 2006
L88          12 DUP REM L7 L11 L87 (2 DUPLICATES REMOVED)
                     ANSWERS '1-2' FROM FILE CAPLUS
                     ANSWERS '3-8' FROM FILE BIOSIS
                     ANSWERS '9-12' FROM FILE WPIX
                D IBIB ED AB L88 2-8
                D IBIB AB ABEX L88 9-12

     FILE 'CAPLUS' ENTERED AT 13:18:00 ON 14 SEP 2006
                D QUE L50
                D QUE L51
L89           5 SEA ABB=ON  PLU=ON  (L50 OR L51) NOT L7

     FILE 'BIOSIS' ENTERED AT 13:18:34 ON 14 SEP 2006
                D QUE L21
                D QUE L61
L90          19 SEA ABB=ON  PLU=ON  (L21 OR L61) NOT L11

     FILE 'MEDLINE' ENTERED AT 13:19:18 ON 14 SEP 2006
                D QUE L69

     FILE 'EMBASE' ENTERED AT 13:19:31 ON 14 SEP 2006

     FILE 'EMBASE' ENTERED AT 13:19:49 ON 14 SEP 2006
                D QUE L70
                D QUE L75
L91           9 SEA ABB=ON  PLU=ON  L70 OR L75
```

```
     FILE 'WPIX' ENTERED AT 13:21:53 ON 14 SEP 2006
                D QUE L82
                D QUE L85
                D QUE L87
L92              8 SEA ABB=ON  PLU=ON  (L82 OR L85 OR L87) NOT L40

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, WPIX' ENTERED AT 13:23:53 ON 14
     SEP 2006
L93             37 DUP REM L69 L89 L90 L91 L92 (5 DUPLICATES REMOVED)
                       ANSWER '1' FROM FILE MEDLINE
                       ANSWERS '2-5' FROM FILE CAPLUS
                       ANSWERS '6-24' FROM FILE BIOSIS
                       ANSWERS '25-30' FROM FILE EMBASE
                       ANSWERS '31-37' FROM FILE WPIX
                D IBIB ED ABS L93 1-30
                D IBIB AB ABEX L93 31-37


     FILE HOME

     FILE CAPLUS

     Copyright of the articles to which records in this database refer is
     held by the publishers listed in the PUBLISHER (PB) field (available
     for records published or updated in Chemical Abstracts after December
     26, 1996), unless otherwise indicated in the original publications.
     The CA Lexicon is the copyrighted intellectual property of the
     American Chemical Society and is provided to assist you in searching
     databases on STN.  Any dissemination, distribution, copying, or storing
     of this information, without the prior written consent of CAS, is
     strictly prohibited.

     FILE COVERS 1907 - 14 Sep 2006  VOL 145 ISS 12
     FILE LAST UPDATED: 13 Sep 2006  (20060913/ED)

     Effective October 17, 2005, revised CAS Information Use Policies apply.
     They are available for your review at:

     http://www.cas.org/infopolicy.html

     FILE BIOSIS
     FILE COVERS 1969 TO DATE.
     CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
     FROM JANUARY 1969 TO DATE.

     RECORDS LAST ADDED: 13 September 2006 (20060913/ED)


     FILE MEDLINE
      FILE LAST UPDATED: 13 Sep 2006 (20060913/UP).  FILE COVERS 1950 TO DATE.

      On December 11, 2005, the 2006 MeSH terms were loaded.

      The MEDLINE reload for 2006 is now (26 Feb.) available.  For details
      on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
      See also:

         http://www.nlm.nih.gov/mesh/
         http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
         http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
```

http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE EMBASE
FILE COVERS 1974 TO 14 Sep 2006 (20060914/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE WPIX
FILE LAST UPDATED: 11 SEP 2006 <20060911/UP>
MOST RECENT DERWENT UPDATE: 200658 <200658/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE, PLEASE VISIT:
http://www.stn-international.de/training_center/patents/stn_guide.pdf <

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE
http://scientific.thomson.com/support/patents/coverage/latestupdates/

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE
http://www.stn-international.de/stndatabases/details/ipc_reform.html and
http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf <<<

>>> FOR FURTHER DETAILS ON THE FORTHCOMING DERWENT WORLD PATENTS INDEX ENHANCEMENTS PLEASE VISIT:
http://www.stn-international.de/stndatabases/details/dwpi_r.html <<<

=>